EXHIBIT H

REDACTED

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

- - -

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION : MDL No. 2875

THIS DOCUMENT APPLIES TO ALL CASES : HON ROBERT B. KUGLER

- - -

CONFIDENTIAL INFORMATION - SUBJECT TO PROTECTIVE ORDER

MARCH 21, 2022

- - -

Remote Videotape Deposition, taken via Zoom, of ERIC SHEININ, Ph.D., commencing at 9:35 a.m., on the above date, before Amanda Maslynsky-Miller, Realtime Reporter and Certified Court Reporter in and for the State of New Jersey.

- - -

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I N D E X

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Testimony of: ERIC SHEININ, Ph.D.

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E X H I B I T S

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None

(It is hereby stipulated and agreed by and among counsel that sealing, filing and certification are waived; and that all objections, except as to the form of the question, will be reserved until the time of trial.)

VIDEO TECHNICIAN: Good morning. We are now on the record. My name is Chris Clee, I'm a videographer for Golkow Litigation Services. Today's date is March 21st, 2022, and the time is 9:35 a.m. Eastern Standard Time.

This remote video deposition is being held in the matter of valsartan, Losartan and Irbesartan Products Liability Litigation, MDL Number 2875. The deponent is Eric Sheinin.

All parties to this

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deposition are appearing remotely and have agreed to the witness being sworn in remotely.

Due to the nature of remote reporting, please pause briefly before speaking to ensure all parties are heard.

Counsel will be noted on the stenographic record. The court reporter is Amanda Miller, who will now swear in the witness.

- - -

ERIC SHEININ, Ph.D., after having been duly sworn, was examined and testified as follows:

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EXAMINATION

- - -

BY MR. DAVIS:

Q. Good morning, Dr. Sheinin. My name is John Davis, I'm at the law firm of Slack Davis Sanger down here in Austin, Texas.

How are you doing this

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morning?

A. Okay, John. I'm doing all right, thank you. How are you?

Q. Good. Not too bad. We're braving some tornado warnings and severe hail threats here, so hopefully we'll keep power throughout this entire thing.

A. Okay. Good.

Q. Well, let me start by asking you, have you ever given testimony under oath before?

A. Yes, I have.

Q. Okay. About how many times?

A. Five or six, I think.

Q. Would that have been in the capacity of an expert witness each of those times?

A. I guess so. One of the times I was still at FDA, and I was -- what I was asked to talk about, it was a device/drug combination. And I had to talk about the -- one of the chemicals in the -- in the device/drug combination.

And I guess -- I wasn't

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necessarily called an expert witness, but I was doing it as part of my job at FDA.

Q. Okay. Would that have been in a court proceeding or some kind of regulatory --

A. It was a deposition.

Q. -- proceeding?

A. It was a deposition.

Q. Okay. The underlying sort of proceeding that the deposition occurred in, would that have been a court case or some kind of regulatory action?

A. I think it was regulatory. I don't believe it was in a court action.

Q. Do you recall what the device/drug combo was?

A. I'm not sure that I'm at liberty to say.

Q. And then the other -- I think you said five to six times total, once in this FDA proceeding.

The other -- each of the other times would have been as an expert witness?

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A. Yes.

Q. Can you tell me what those instances of you serving as an expert witness in litigation, minus the FDA proceeding, related to?

A. I can tell you that one of them involved a court case in Canada where I -- I did not give a deposition, but I did appear at trial. And that involved how FDA would look at a pure enantiomer, if the original application was for a racemate, what would be expected from the chemistry perspective.

MR. REEFER: John is an expert on that subject, aren't you, John?

BY MR. DAVIS:

Q. I think I'm going to defer to you on all those chemistry terms and just say, that was a -- mostly a scientific-based expert opinion as a process chemist?

A. Not as a process chemist, just as a review chemist and how -- how

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FDA would -- what FDA would want in the application if it was a single enantiomer versus what was -- what was already approved as a racemate.

Q. Okay.

A. It didn't have anything to do with the process.

Q. Well, sure. I guess let me --

A. The regulatory process. Let me say that, yeah.

Q. Right. And that was going to be my question.

The opinion you gave in that was -- was a chemistry-related opinion, not anything really focused on regulatory affairs or anything like that, right?

A. Correct.

Q. Okay.

MR. REEFER: Eric -- can I interject just to help us all out?

Eric, if you could give a second-or-two pause before answering, that would be helpful

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for everybody involved, okay?

THE WITNESS: Okay.

BY MR. DAVIS:

Q. Okay. So I think you mentioned there might be a couple of other times you served as an expert witness.

Can you give me a brief description of those instances as well?

A. One that I'll -- I should wait.

One that I recall was -- it involved a company that received approval for an ANDA, and there was basically a Phase IV commitment that FDA wanted them to do, and there was also litigation that caused the approval to be delayed because of the litigation.

And what I testified to involved a timeline that the company, for whatever reason, delayed doing the work that FDA wanted because they knew there was a litigation and they would not be able to launch the product until a

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certain point in time. And so they basically took their time responding to FDA.

And my part of the -- what I was asked to opine on was what if the company had gone forward and done the work immediately, what would FDA -- how would FDA have looked at the final approval, whether it would have speeded up the -- getting the approval, which, of course, would have been -- the company would have been able to launch sooner.

So it was basically something like that.

Q. And so that, the litigation, underlying litigation, would have been a patent litigation, I suppose?

A. Pardon me?

Q. Was this an instance of what we call delayed generic entry litigation?

MR. REEFER: Object to form.

Go ahead, if you can.

THE WITNESS: I don't know what that -- what that means. But

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the litigation ended sooner than the company expected, so they could have presumably launched sooner if they had done the work sooner.

BY MR. DAVIS:

Q. Who did you represent in that case -- or, sorry, and by "represent," I mean on whose behalf did you submit an expert report?

A. You know, I don't recall which company it was.

Q. Was it a follow-on generic company, like, not the first-file ANDA but a follow-on generic company?

A. I believe it was a first generic.

Q. That company wasn't Mylan, was it?

A. No.

Q. Do you know if it was any of the manufacturer defendants in this valsartan MDL litigation?

A. It was not.

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Q. Okay. Any other instances of serving as an expert witness?
A. Yeah. I recall one, actually, it was a functional food. And my part involved evaluating work that the other side's contract lab had performed, trying to quantify the amount of an impurity that was in the functional food ingredient.
Q. Okay. Any other instances?
A. I believe -- I know there were a couple of others. I can't recall what the specifics were, but it involved chemistry.
Q. What about a Fresenius dialysis product? Did you ever give expert testimony in that -- for Fresenius in that case?
A. I don't believe I ever did anything for Fresenius.
Q. Okay. You don't recall a litigation versus Fresenius in the Northern District of Illinois, Case Number 16-cv-651?

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A. I don't recall. I know I did do a deposition on a case in Chicago, so it might be related to that. But I don't -- I don't recall that -- that I was involved with Fresenius.
Q. In each of those instances of serving as an expert witness, were your reports and opinions tendered on behalf of pharmaceutical manufacturers or device manufacturers in each of those instances, aside from the FDA one?
A. Pharmaceutical manufacturers.
Q. When were you engaged by Mylan for this case?
A. I believe it was late 2021.
Q. By "late 2021," can you give a month?
A. November or December.
Q. I noticed on a couple of your invoices that the invoices were submitted from an entity called ProPharma Group.
Who are they?

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A. I'm not sure all the -- represent -- how it all came about.
But it's, basically, I'm doing work through NDA Partners. And NDA Partners has merged a couple of times. So I still look at everything I'm doing as through NDA Partners. So I guess ProPharma is maybe now the parent.
Q. Does either ProPharma or NDA Partners take a cut of your expert witness fees?
A. Yes, they do.
Q. What is that percentage?
A. I don't know what the percentage is, but I get $400 an hour.
Q. Okay. Just to get a little background on you, Dr. Sheinin, can you give me a brief rundown of your professional career as relates to FDA, USP, and then your work in the consulting industry?
A. Sure. I received a Ph.D. from the University of Illinois, College of Pharmacy, in organic chemistry in

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1971.
And I worked for FDA beginning in February of 1971, in the division of drug chemistry. I was a research chemist. I was doing work on nuclear magnetic resonance to identify unknown samples and to develop analytical methods to quantify the content of pharmaceutical products.
Within a couple of years of joining FDA, we bought our first mass spectrometer on the drug side, and I helped to run that instrument along with another chemist who had come from a different agency who was a mass spectrometrist.
And between the two of us, we published a number of papers, both using NMR and using mass spec. We were able to couple a gas chromatograph to the mass spectrometer, and we did do research and -- trying to identify unknown materials that FDA field labs were not able to handle.

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Around 1978 or so, we had four branches in the division of drug chemistry. And one of the branch chiefs passed away. I competed for that position and was selected to become a branch chief.

And during that -- my time in that position, I was responsible for supervising a group of chemists who, quote/unquote, performed method validation for analytical methods that companies had submitted in their new drug applications to make sure that a competent FDA analyst could run the procedures and come up with results that were comparable to what the company had provided.

We also had somebody in my group who was doing powder -- x-ray powder diffraction studies.

Around 1985 or so, FDA merged the Bureau of Drugs and the Bureau of Biologics. They were called bureaus in those days. And biologics was in

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charge of the combined bureau, and they made the decision, at one point in time, to move some people to the review area, chemists to the review area, because there was a big backlog of new drug applications that were pending chemistry review.

And as it turned out, they closed the entire division of drug chemistry and offered everybody in the division a position in headquarters. And some people took the position, some people retired, and some people took other positions within the government.

I moved to the review area as a supervisory chemist, and I had responsibility, initially, for chemists who were reviewing anti-inflammatory drug applications on the new-drug side. This was in the division of oncology and radiopharmaceuticals.

It was the first division that had two supervisory chemists, and eventually the responsibility ended up

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for all the drugs within the division. So I took over the oncology drugs and the radiopharmaceuticals, which included other imaging agents as well.

The bureau -- well, this was now, then, the Center of Drug Evaluation and Research. And there was a reorganization that took place, and what was created was the Office of Pharmaceutical Science.

And within the Office of Pharmaceutical Science, there were four smaller offices. One was the Office of New Drug Chemistry. And I competed for one of the three branches -- or one of the three divisions within that office. The Office of New Drug Chemistry had three divisions. And I was selected as one of the division directors, the Division of New Drug Chemistry 3.

And within that office, then, Roger Williams, who was the head of the office of -- Office of Pharmaceutical Science, was also acting as director of

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the Office of New Drug Chemistry.

The three division directors -- as I mentioned, there were three divisions. The three of us competed for the permanent position of director of the Office of New Drug Chemistry, along with approximately 80-some people from the outside.

I was selected to lead the division of -- the Office of New Drug Chemistry. And I worked in that position for approximately two years, and then I moved up to be the deputy director in the Office of Pharmaceutical Science, which was what was termed a super office versus the smaller offices. I stayed in that position for approximately one year.

When I reached 30 years at FDA, I was able to retire with a full -- a full pension, and I decided to move to USP.

My boss at FDA, Roger Williams, had left the year prior to my retirement, and he went to USP as the

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chief executive officer, executive vice president. And he recruited me to move to USP as a vice president.

And I had responsibility for the scientists at USP who were responsible for creating content of USP and NF, working with expert -- volunteers on expert committees as well as the pharmaceutical industry and, at times, academia.

USP had a program to verify the quality of dietary supplement ingredients, and eventually they moved into dietary supplement products. And Roger Williams wanted to start a program to evaluate the quality of active pharmaceutical ingredients or drug substances.

And I moved to that area, and I worked on trying to recruit companies to submit their DMFs or just their procedures for their drug substances.

And after working for about

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a year on that side, I felt, if I was ever going to go into consulting, which was something I had thought about when I retired from FDA, that now was the time, I was still young enough. And I went into consulting.

And that's kind of a nutshell of what my career has been. I've been consulting since March of 2007.

Q. Okay. Thank you for that. And I'll take a few questions just in order.

You mentioned Roger Williams, who was your former boss at FDA, right?

A. Yes.

Q. Are you aware that he's submitted an expert report in this case?

A. I'm not aware.

Q. So you would not have talked to him or e-mailed with him about that at all?

A. No, I have not.

Q. Have you communicated with

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any of the other defense experts who have submitted opinions in this litigation?

A. I have not.

Q. You mentioned a -- and so just a clarification on a few dates.

I think you said you retired from FDA after 30 years, but you didn't give a date. I assumed that means 2001, if you started in 1971?

A. Yes. The end of February 2000 -- 2001.

Q. Okay. And then when did you -- so you went to USP in 2001 as well?

A. Yes. March of 2001. I think I had two weeks --

Q. And then --

A. -- two weeks in between.

Q. Got you.

And then you retired from USP around 2007-ish?

A. Yes.

Q. You mentioned trying to recruit companies to submit their DMFs or

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drug substance manufacturing procedures to USP.

Would that be for pharmaceutical drugs, or was that in the context of dietary supplements?

A. No, this was pharmaceutical ingredients. For the most part, companies were reluctant to get into it because FDA was the legal authority.

There was a -- the European Pharmacopoeia, through the European Directorate for the Quality of Medicines, had a program that actually was required, through EMA, to -- for companies to submit their active ingredients for evaluation.

And I believe Roger was interested in getting into the same type of -- same type of program. But I don't believe that FDA would ever have given up the responsibility for evaluating the chemistry of the -- of active pharmaceutical ingredients or drug substances.

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Q. In your consulting work since 2007, have you -- have you always consulted for industry?
MR. REEFER: Object to form.
THE WITNESS: I have given some advice, a couple of times, to academia. And I also did some training for USP. I did some training courses that USP offered.
BY MR. DAVIS:
Q. What percentage would you say, of your consulting work since 2007, has been for industry?
A. Probably 98 percent or more.
MR. DAVIS: I'm going to mark your report, Dr. Sheinin.
That's Tab 1, Jason, in the box, if he doesn't have a copy.
MR. REEFER: John, I'm going to stand up, and I'm going to be off camera for a moment.
MR. DAVIS: Sure.
MR. REEFER: Actually, just give me one second, okay?

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For purposes of formality, John, you see me now?
MR. DAVIS: Yes.
MR. REEFER: I just wanted you to see that we have not yet opened the box. So just give me one moment, okay? I have scissors.
MR. DAVIS: Not a problem.
MR. REEFER: Tape must have been on sale at Costco when you packaged this.
Tab 1, John?
MR. DAVIS: Tab 1.
- - -
(Whereupon, Exhibit Sheinin-1, No Bates, Expert Report of Eric Sheinin, Ph.D., was marked for identification.)
- - -
BY MR. DAVIS:
Q. Dr. Sheinin, do you recognize what's been handed to you as Exhibit-1 -- that I've now marked as

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Exhibit-1 as your expert report in this case?
A. Yes.
Q. In coming up with your expert report, did you review at all Federal Rule of Civil Procedure 26, which governs the disclosure of expert reports in federal court litigation?
A. No, I have never seen that.
Q. Well, I'll just tell you that that rule states that, and I'm quoting, The report must contain a complete statement of all opinions the witness will express and the basis and reasons for them.
Did you -- did you hear that sentence well?
A. Yes.
Q. Okay. Do you feel that your expert report that you've submitted in this case complies with what that rule requires, namely, a complete statement of all your opinions and the basis and reasons for them?

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MR. REEFER: Object to form. Calls for a legal conclusion.
THE WITNESS: Yes.
BY MR. DAVIS:
Q. So, in other words, there's no opinions in your -- that aren't in your report that you would be seeking to express in this litigation, correct?
MR. REEFER: Object to form.
THE WITNESS: Yes.
BY MR. DAVIS:
Q. "Yes" meaning that there are no other opinions that you're trying to assert in this litigation that you have not put in your expert report?
MR. REEFER: Object to form.
THE WITNESS: That's correct.
BY MR. DAVIS:
Q. Turn, if you would, to the second page of your report at Paragraph 8.
You state there, I offer the opinions set forth in this report to a

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reasonable degree of scientific certainty based on my education, experience, training, expertise and referenced resources.

Do you see that?

A. Yes.

Q. I just want to get some clarification of what you mean by "referenced resources."

What are you referring to there?

A. I actually copied this beginning from another expert report, and I did not think about what referenced resources I was -- what referenced resources this referred to.

But I would assume it would be things like the USP, the NF, FDA guidances, ICH guidances, documents like that.

Q. Did you write this report with a degree of care, Dr. Sheinin?

A. Yes.

MR. REEFER: Object to form.

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THE WITNESS: A lot of care.

BY MR. DAVIS:

Q. But what you're telling me is that you're not sure what you mean by "referenced resources" there because you copied it from another expert report of yours?

MR. REEFER: Object to form. Mischaracterizes testimony.

THE WITNESS: I tried to explain what I would consider referenced resources. And I would still say the same thing.

I would consider these referenced resources things such as USP, the NF, FDA guidances. I might add FDA policies and procedures, ICH guidances. That -- to me, that's what referenced resources would be.

BY MR. DAVIS:

Q. Okay. Well, referenced resources means resources that are referenced, right?

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Are there any resources that you relied on that aren't -- are not referenced in your report somewhere, either in a footnote or your materials considered list, I believe which is Exhibit B, as you state in Paragraph 7?

A. I don't believe there are any others.

Q. So would I be correct in making the assumption that if there's something that's not referred to somewhere in your report, that you didn't consider it in coming to your opinions?

MR. REEFER: Object to form. Mischaracterizes testimony.

THE WITNESS: Can you repeat the question?

BY MR. DAVIS:

Q. Sure.

Would I be correct -- what I'm trying to do, Dr. Sheinin, is sort of, you know, capture the view of everything you reviewed for your expert report in this case. And normally that's

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through either footnoting it as citations in the body of your report or discussing it explicitly in your report or referencing a list of materials that you considered or looked at in the process of writing it.

And so what I'm trying to do is clarify whether what's in the report is the complete -- you know, wherever it is in your report, that that's a complete list of everything you looked at in writing your report.

Do you follow?

MR. REEFER: Object to form.

THE WITNESS: I follow. And I believe that's the situation.

BY MR. DAVIS:

Q. I just referenced Paragraph 7. You write there that, A list of materials provided for my consideration is attached as Exhibit B.

Do you see that?

A. Yes.

Q. Were those materials

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provided by counsel?
A. Yes.
Q. Did you ask for them specifically or was it just a package that was given to you?
A. I believe it was a package that was given to me.
Q. Did you ask counsel or make any inquiries as to whether there was anything additional that you might want to look at?
A. I don't recall asking for other things.
Q. So you just trusted that what was given to you by Mylan's counsel was a complete picture of the relevant information that you might want to look at?
MR. REEFER: Object to form.
THE WITNESS: I was asked to opine on how USP functions and what drug master files are. Anything that I looked at that counsel provided was to get a

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background for the overall picture.
But I used my background and my expertise and experience at USP and at FDA to create my report.
BY MR. DAVIS:
Q. Well, my question was whether you trusted that what was given to you was a complete picture, including for those topical areas you just referenced, such as USP and drug master files.
Is that --
MR. REEFER: Object to form.
Asked -- sorry, John.
BY MR. DAVIS:
Q. Did you trust that what was given to you by Mylan's counsel painted a complete and accurate picture for you?
MR. REEFER: Object to form.
Asked and answered.
THE WITNESS: What -- my background, I believe, was sufficient for me to give my

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opinion on USP and FDA's consideration of drug master files.
Anything that I looked at that counsel had provided, as I mentioned, was to provide a background understanding of -- basic understanding of the issue. It was nothing that I considered in -- that I would have incorporated into my report.
I would have to venture to say that I would -- I would think that the amount of material that I received from counsel is a very, very, very small proportion of the documents that might have been used to fully explain the situation.
I just can't imagine that if -- if counsel had provided me everything that is included in the court proceedings, it probably would have more than filled up my

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office.
So I just don't understand what -- what the question is getting at.
BY MR. DAVIS:
Q. Well, sure, let me ask it, I suppose, in a different way, then, which is, did you -- upon receiving the information that is listed at Exhibit B of your report, upon reviewing that, did you ever go back to counsel and ask for anything else?
A. I'm turning the page.
Actually, I may have asked for the response -- Mylan's response to the warning letter. I can't recall for definite whether that was included in the original group.
Q. Did you ask -- sorry. Go ahead, Dr. Sheinin. I didn't mean to cut you off there.
A. I think I may have asked for that response to the warning letter.
Q. Why would you have asked for

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that?
A. Just to get an overall picture of how Mylan responded.
Q. And by "warning letter," you're referring to the November 2019 warning letter issued to Unit 8?
A. Yes.
Q. While we're discussing that, real fast, and we may come back to it, but what's your understanding of how the FDA received Mylan's response to the warning letter?
MR. REEFER: Object to form. Beyond the scope. Lack of foundation.
THE WITNESS: I am -- I can't say how FDA responded. I have not seen anything in writing from FDA about the response.
But I do know that Mylan -- Mylan's valsartan products are back on the market, so I would have to assume that the -- that FDA was satisfied with their

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response, and that's how -- that's why the products are on the market again.
BY MR. DAVIS:
Q. Well, do you understand that the warning letter had to do, for Unit 8, in part, with Mylan's practices around recovered solvents and --
MR. REEFER: Object to form as beyond the scope.
BY MR. DAVIS:
Q. -- as well as the issue of the nitrosamine contamination in the first place?
MR. REEFER: Object to form. Beyond the scope. Compound. And mischaracterizes the document.
THE WITNESS: That is the -- the response from Mylan to FDA is not the basis of my report.
So I consider that to be -- it was irrelevant as to whether -- is irrelevant in terms of how FDA might have responded to Mylan's

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response.
It doesn't form the basis for anything that's in my report.
BY MR. DAVIS:
Q. Did you ask counsel to see a copy of the FDA's close-out letter for Mylan's warning letter?
A. I don't believe I did.
Q. Do you know if one exists?
A. I do not know.
Q. So you wouldn't know if that warning letter remains unresolved to this day?
MR. REEFER: Object to form. Beyond the scope. Lack of foundation.
THE WITNESS: I have no way of knowing whether it still exists or not.
BY MR. DAVIS:
Q. Okay. And you mentioned Mylan having a -- bringing valsartan back to the market, correct?
A. As far as I know,

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valsartan -- Mylan's valsartan products are on the market.
Q. Do you know if Mylan had to commit to the FDA not to use recovered solvents until they could ensure that they were safely used and that --
MR. REEFER: Object to form. I'm sorry, John.
BY MR. DAVIS:
Q. Sorry. Let me start that question over, Dr. Sheinin.
Do you know if -- let me break it down into bits.
Do you know if Mylan's valsartan product that's back on the market today is manufactured using recovered solvents?
MR. REEFER: Object to form. Beyond the scope. Lack of foundation.
THE WITNESS: That's something I don't have knowledge of. It's -- again, it's not something that I used to create my

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report. Whether or not they're using recovered solvents, I can't tell you that. I don't know.
BY MR. DAVIS:
Q. Okay. Do you know if Mylan had to change the process chemistry of its valsartan API to bring it back to the market?
MR. REEFER: Object to form. Beyond the scope. Lack of foundation.
THE WITNESS: I'm not a process chemist, so it's very hard for me to answer that question. It's a very specialized area.
I've never worked in the pharmaceutical industry, never worked in developing a process for manufacturing of a drug substance. And it's not something that I can opine on.
BY MR. DAVIS:
Q. Okay. But you're not -- you're not aware, for example, of whether

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Mylan had to remove its use of triethylamine and substitute it with sodium bicarbonate in an effort to avoid NDEA or other nitrosamine contamination in order to bring valsartan back to the market?
MR. REEFER: Object to form. Compound. Beyond the scope. Lack of foundation.
THE WITNESS: Again, I'm not a process chemist, and I would not attempt to try to interpret or understand what processes Mylan used.
I did not consider whether or not there was a change in the manufacturing process to form the basis for my report. And that's -- I use my experience at USP and at FDA to create the report.
So it's beyond my understanding of process chemistry, which is essentially

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nothing. It's beyond my expertise.
BY MR. DAVIS:
Q. Well, sure, and I'm only asking this because you brought up the fact that Mylan has a valsartan product back on the market.
And my question is, are you familiar at all with the circumstances by which Mylan was able to bring a valsartan product back to the market?
MR. REEFER: Same objection.
THE WITNESS: Again, I'm not a process chemist. And it's just beyond what my expertise is. I did not use any of that type of information to form the basis for my report.
BY MR. DAVIS:
Q. Okay. So is the answer no, you're not familiar with the circumstances by which Mylan was able to bring a valsartan product back to the market?

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A. It's -- I'm not a process chemist, and understanding the -- what would go into changing, if that's what occurred, changing the manufacturing procedures is not something that I'm qualified to evaluate.
And I'm going to have to stand on that, that it's nothing that I used in my report.
Q. Well, my question isn't, you know, calling for any kind of process chemistry. I'm just asking what you reviewed.
And my question is, did you review any documents or anything related to how Mylan was able to bring a valsartan product back to the market?
A. My -- again, I'm not a process chemist. So I -- as to what was involved and how much work was involved, I can't really opine on that.
Q. What about concessions to the regulator, are you familiar with any concessions Mylan had to make to the

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regulator, the FDA, in order to bring a valsartan product back on the market?

MR. REEFER: Object to form. Vague. Beyond the scope. Lack of foundation.

THE WITNESS: I am -- I am -- let me start over.

I am -- I don't know what -- I'm not a process chemist, and I just feel that whatever Mylan did to get on the market is beyond what I was asked to look at and what I was asked to opine on.

I used my expertise and my background at USP and FDA to create my report. Anything else was immaterial to providing my opinions that are in my report.

BY MR. DAVIS:

Q. Okay. Well, let me ask it this way, then: Is the fact that Mylan is back on the market with a valsartan product, under circumstances that you don't know or understand, that's not

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relevant to any of the opinions in your report, is it?

A. I don't believe so.

Q. Okay. Thank you.

You list the ANDAs in Exhibit B to your report, do you not?

A. Yes, I do list them.

Q. Do you understand that those ANDA applications all made reference to a drug master file?

A. Yes.

Q. Did you review the full drug master file?

A. I didn't review any part of the drug master file.

Q. Okay. So that was my question.

So you reviewed the ANDA applications but not the underlying drug master file that those ANDAs made reference to?

A. I glanced at one of the ANDAs. I did not review all three of them. And what I saw was mostly -- at

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least the portions of the requirements in the ANDA for the drug substance made reference to the drug master file.

So there was very little information in the ANDA itself, and I did not pursue asking counsel to provide me the DMF because I felt it was irrelevant to what my part of the -- creating my report was.

I was just -- the ANDAs were there and I thought I probably ought to take a look at them, but there was really nothing for me to understand. And I just said, I don't need that information to create my report on how USP operates and what a drug master file is. So I did not pursue it.

Q. Well, that's my -- you kind of touched on my next question, which is, you told me your assignment was to opine on USP and drug master files.

But you didn't think to ask Mylan for the drug master file that's at issue in this case?

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A. I did not because I was giving, in my expert report, a general overview of drug master files. I was not asked to opine on the quality or the content of Mylan's drug master file, so it was irrelevant.

Q. Okay. That -- let me clarify exactly what your assignment was in this case, then, because it's nowhere written in your report what your assignment was.

And to be honest, I'm a little confused, because you're telling me your assignment was to opine on drug master files generally but not to opine on Mylan's drug master file in any way in this case; is that right?

A. That's correct. I was not asked to opine on the quality of Mylan's drug master file.

Q. And you did not, in fact, opine on the quality of Mylan's drug master file in your report, did you?

A. I couldn't. Because, one, I

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wasn't asked to; and, two, I never saw the drug master file.
Q. So since it's written nowhere in your report, can you tell me exactly what your assignment was in this case?
A. My assignment was to -- the basic part of my assignment, the bulk of it, was to talk about USP and the background of USP, in terms of how USP is organized, USP's recognition in the Food, Drug and Cosmetic Act, and to give a brief description, discussion of drug master files and why -- why there are drug master -- I talked about why there are drug master files, types of drug master files and so on.
I was also asked to comment on Dr. Najafi's expert report.
Q. Were you asked to comment on John Quick's expert report?
A. I was asked if I -- if I -- if I wanted to comment on John Quick's, as well as Najafi, but I felt that

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Quick's was more involved with GMPs and, that was not my area of expertise at FDA. So commenting on Najafi was more in line with the function of my report and the expertise that I have.
Q. Okay.
MR. DAVIS: I'm going to mark Tab 2 as Exhibit-2, Jason.
- - -
(Whereupon, Exhibit Sheinin-2, No Bates, 1/12/22 Letter, Trischler to Counsel, was marked for identification.)
- - -
MR. REEFER: Okay.
BY MR. DAVIS:
Q. Dr. Sheinin, this was a letter from Jason's law firm that accompanied the disclosure of your expert report.
Do you understand that?
MR. REEFER: Object to form. Why don't you start by asking if he's seen it before?

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BY MR. DAVIS:
Q. Have you seen this letter before?
A. I've not seen this letter before, and I have never seen a letter that looks like this.
Q. Well, yeah, let me just represent to you, then, that this was a letter from Jason's law firm that was delivered to us accompanying your expert report.
Do you see that your name is referenced in there and it's addressed to a number of plaintiffs' counsel in this case?
MR. REEFER: Object to form. Lack of foundation.
THE WITNESS: I see that my name is on here, yes. And it's --
BY MR. DAVIS:
Q. Okay.
A. -- talking about my expert report is also enclosed.
Q. If you look down at

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Paragraph 2, it says that your report is, For purposes of rendering opinions as to class certification issues and rebutting the class certification opinions of the class certification experts disclosed by the plaintiffs' executive committee.
Do you see that?
A. I see it.
Q. Do you know what class certification issues you address in your report?
MR. REEFER: Object to form. Beyond the scope. Calls for a legal conclusion.
THE WITNESS: I don't know what "class certification" means.
BY MR. DAVIS:
Q. And the second part of that is to rebut the reports of the plaintiffs' experts.
In your case, that's only Dr. Najafi; is that right? Is that your testimony?
MR. REEFER: Object to form.

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Mischaracterizes testimony.
THE WITNESS: I discuss Dr. Najafi's report in my report, yes.
BY MR. DAVIS:
Q. And there's no other plaintiffs' expert report that you both reviewed and intend to rebut in your report, is there?
MR. REEFER: Object to form. Foundation.
Go ahead, Doctor.
THE WITNESS: That's correct.
BY MR. DAVIS:
Q. You mentioned, Dr. Sheinin, that your educational background is that you have a Ph.D. in organic chemistry; is that right?
A. That's correct.
Q. Can you, at a very broad level, speaking to a -- most certainly a non-expert like me and Jason --
MR. REEFER: That's right.

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BY MR. DAVIS:
Q. -- tell us -- tell us what organic chemistry is?
A. Organic chemistry is, in the briefest of statements, is the chemistry of carbon compounds. That's probably the easiest way to explain it.
There's different classes of chemicals that are considered organic. There's various functional groups.
I can't say 100 percent that every organic chemical contains carbon, but, for the most part, that's -- that's true. And it's -- involves reactions using other organic chemicals as well as non-organic chemicals to manufacture or synthesize a second organic chemical and sometimes maybe a third and a fourth.
That's what my -- my Ph.D. thesis involved synthesizing a number of compounds that were subsequently sent to the National Cancer Institute for testing for activity against -- against cancer. And, unfortunately, none of the chemicals

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I manu -- I synthesized had any activity.
I always felt that I was going to get a job working for somebody who is doing organic chemistry. That turned out not to be the case. When I joined FDA, we had an organic chemist in our group, and he actually worked as a functioning organic chemist. I have never worked as a functioning organic chemist.
So it's -- I think it's something that is fairly common, certainly it is among people that I knew who went to graduate school with me, they don't necessarily end up working in what your major was.
So I'm more of an analytical chemist with knowledge of regulatory. But I've never worked as an organic chemist.
Q. Right. In fact, I think, you know, in your brief FDA history you gave me, your work with mass spec and GC -- you know, coupling it with a GC in

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the early '70s, that's more analytical chemistry, right?
A. Yes.
Q. So harkening back to your dissertation thesis days when you synthesized a few compounds with the hopes that they might have an effect on cancer, did you work in the lab at all in, you know, synthesizing those -- creating those chemical reactions to synthesize those compounds?
A. Oh, yeah. I mean, that's how I got the compounds.
Q. So in working with -- would you have worked with, like, reagents, catalysts, solvents, all that business, in order to create those chemical reactions that would ultimately yield the compound you wanted to create?
MR. REEFER: Object to form.
THE WITNESS: Yes. I did the synthesis myself.
BY MR. DAVIS:
Q. So how would you know, in

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doing that, what to avoid mixing together to create a dangerous reaction? What kind of materials would you look at, aside from just your own educational knowledge of how these substances interact?

MR. REEFER: Object to form. Beyond the scope.

THE WITNESS: I relied on my advisor to give me advice on if there was any danger or any possible reactions that he considered to be dangerous.

BY MR. DAVIS:

Q. Did you rely on any kind of written materials in addition to just what your advisor told you?

MR. REEFER: Object to form. Beyond the scope.

THE WITNESS: You know, that's over 50 years ago, and I can't remember if there was anything written or not. But I relied on my advisor.

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BY MR. DAVIS:

Q. Okay. Do you know what an MSDS is?

A. Yes, I do.

Q. Like a safety data sheet for a particular substance?

A. Yes.

Q. Okay. Is that something that -- would those have existed at that timeframe?

A. As far as I can remember, I don't believe there were safety data sheets at that time.

Q. If you were doing that kind of organic chemistry today, is that something you might want to look at, the safety data sheets or MSDS?

MR. REEFER: Objection. Form. Incomplete hypothetical. Beyond the scope.

THE WITNESS: I mean, if I was doing organic chemistry today, I would want to know if there was any safety issues with the

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materials that I'm working with. It's something that did not exist in those days.

BY MR. DAVIS:

Q. And if you were doing that today, one of the most prominent resources you could -- you could consult would be the safety data sheet, or MSDS, that accompanies whatever reagent or catalyst it is that you're working with, right?

MR. REEFER: Object to form. Beyond the scope. Incomplete hypothetical.

THE WITNESS: I would have to assume that I would look at those, at least once, for any chemical that I work with. I wouldn't have to keep going back to look at them.

BY MR. DAVIS:

Q. Okay.

MR. REEFER: Hey, John, this is Jason. I had a venti coffee

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this morning. We've been going about an hour and 20 minutes. Would you mind just taking a five-minute bathroom break?

MR. DAVIS: Sure. Not a problem.

Dr. Sheinin, do you need five minutes or ten minutes? Up to you.

We can go off the record, by the way.

VIDEO TECHNICIAN: Going off the record. The time is 10:50 a.m.

- - -

(Whereupon, a brief recess was taken.)

- - -

VIDEO TECHNICIAN: We are back on the record. The time is 11:00 a.m.

BY MR. DAVIS:

Q. Just one clean-up question, Dr. Sheinin, before I move on.

Do you recall telling me that you're not a CGMP expert?
A. Yeah, I recall.
Q. Okay. So would I take that to mean that you're not offering any opinion in this litigation that Mylan was, in fact, in compliance with CGMPs?
A. I'm not offering an opinion directly on whether they're in compliance with GMPs. I know that their product is on the market. I know that FDA has inspected their facilities. And I know there was a warning letter, and I know that they're back on the market.
That's pretty much beyond what I know about Mylan and their GMPs.
Q. But just to clarify, you're not offering any kind of expert opinion in this litigation that Mylan was in compliance with CGMPs, despite stuff that's tangential to that that you've reviewed, correct?
A. My expert report is discussing drug master files and USP. It

does not discuss GMPs. I'm not a -- I'm not -- as I said and you agreed, I'm not an expert in GMPs, and I'm not offering to opine on it.
Q. So, for example, you said you reviewed the FDA warning letter issued to Mylan Unit 8, which manufactured valsartan API; isn't that right?
A. I looked at it. I wouldn't necessarily say -- I did not review it in depth. It was not something that I needed for forming my opinions in my expert report. But I did look at it.
Q. Right. And would you have seen the statement at the beginning of that letter that the FDA observed CGMP deviations at that facility, which was the -- you know, the reason they were sending the warning letter?
MR. REEFER: Object to the form. Calls for speculation.
Go ahead --
MR. DAVIS: Well, I'm not

asking -- well, hang on, Jason, I'm not asking him to speculate. I'm just asking if he saw that statement in the letter that he reviewed.
BY MR. DAVIS:
Q. Do you recall seeing that statement in the letter that you -- in the warning letter, Dr. Sheinin?
A. I recall the warning letter. Can you put it up on the screen?
Q. Sure.
A. So I can see the exact language. Or do we have it in our -- in our package?
Q. Just a second, I'll bring it up.
MR. REEFER: Do you have it as an exhibit, John?
MR. DAVIS: Yes. That would be Tab 15.
MR. REEFER: One moment, okay?
MR. DAVIS: Yep.

- - -
(Whereupon, Exhibit Sheinin-3, MYLAN-MDL2875-003457, 11/5/19 FDA Warning Letter, was marked for identification.)
- - -
MR. DAVIS: I'm marking that as Exhibit-3.
MR. REEFER: John, I'm not sure if there's a question pending. I'm sorry.
MR. DAVIS: Sure.
BY MR. DAVIS:
Q. Do you have the letter in front of you, Dr. Sheinin?
A. I do.
Q. Do you recognize that to be a copy of the November 5th, 2019, Unit 8 warning letter that you reference in Exhibit B to your report?
A. Yes.
Q. And do you see the third paragraph -- second and third paragraph down, This warning letter summarizes

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significant deviations from CGMP for APIs. And, Because your methods and facilities and controls for manufacturing processing, packing or holding do not conform to CGMP, your API are adulterated.

Do you see those statements?

A. I see them.

Q. And because you're not offering any kind of opinion that Mylan was, in fact, in GMP compliance, you don't take any issue with what the FDA says here, do you?

MR. REEFER: Object to form. Mischaracterizes testimony.

THE WITNESS: This -- this Paragraph 2 and Paragraph 3, I would say probably Paragraph 4, with different dates is pretty much standard boilerplate language that's in every warning letter.

Mylan's valsartan product is on the market, it's in conformance with the requirements of the USP

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monograph for the API, as well as for the tablets. And the fact that this language is in here, it's in every warning letter that I've seen.

BY MR. DAVIS:

Q. Well, just like with your report, Dr. Sheinin, you have some stock language, for example, that we went over this morning.

It doesn't make it any less true, right? It doesn't mean that the -- just because it's in every FDA warning letter doesn't mean that this one issued to Mylan, the FDA doesn't mean it when they say that Mylan was not in GMP compliance at Unit 8, correct?

A. This is -- again, it's boilerplate language that's in every letter, every warning letter. The fact that FDA has allowed Mylan to come back on the market, has not withheld anything from Mylan, there are no import alerts that -- over Mylan, and the fact that

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this is -- again, like in my report, this is boilerplate language. It's nothing that forms the basis for my report.

Q. So should I -- should I give, for example, the boilerplate language in your report less stock somehow, or should I take that to actually be language in your report?

MR. REEFER: Object to form. Compound. Vague.

THE WITNESS: You can -- you can use that language in my report in any way you like. It's --

BY MR. DAVIS:

Q. Well, I'm asking -- I'm asking your opinion, Dr. Sheinin.

Are you telling me that the language that you cribbed from an old report, I should put less stock into simply because you --

MR. REEFER: Object to form.

BY MR. DAVIS:

Q. -- simply because it's boilerplate?

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MR. REEFER: Object to form. Argumentative. Mischaracterizes the testimony.

THE WITNESS: Again, that's -- it's typical language. It's -- and the boilerplate language here is just boilerplate language.

It's -- the fact that FDA let -- has let Mylan back on the market says to me that whatever deviations there were from current good manufacturing practices are such that FDA feels comfortable with Mylan marketing the valsartan products.

BY MR. DAVIS:

Q. But that's just pure speculation on your part.

You told me, Dr. Sheinin, that you haven't looked at any follow-up on this warning letter to see if it's been closed out; and you told me you have no idea what circumstances Mylan was

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allowed back on the market, right?
MR. REEFER: Object to form. John, you asked him questions about this warning letter and now you're yelling at him for trying to answer them.
MR. DAVIS: Well, no. He's told me, Jason, that he's not a CGMP expert. And I'm just trying to elucidate what he means by that with an example.
And my example here --
MR. REEFER: Right.
MR. DAVIS: -- is in this warning letter that FDA issued to Mylan, the FDA says that there's significant CGMP deviations.
BY MR. DAVIS:
Q. My question to you, Dr. Sheinin, is, are you offering any opinion that Mylan, in fact, during this timeframe, was in CGMP compliance, contrary to what the FDA says in this warning letter?

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MR. REEFER: Object to form. Asked and answered.
THE WITNESS: I'm not offering any opinion, because I'm not a GMP expert.
BY MR. DAVIS:
Q. Okay. Thank you. Thank you.
When did you first learn anything about nitrosamines, Dr. Sheinin?
A. I would have to say probably in 2018 when I heard about the reports of nitrosamines being in certain products, FDA announcements.
I would think that's the first time that I heard -- well, I probably heard about them in graduate school, but that's -- that's neither here nor there.
Q. Well, that's actually --
A. I knew what a nitrosamine was.
Q. Sorry, I didn't mean to cut you off there.

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Go ahead.
A. But the first time I heard about any issues with nitrosamines was in 2018.
Q. Well, my question was actually the more basic one, which is when you first learned what a nitrosamine compound was, not whether there were any issues in medications.
And it sounds like the answer is at some point in graduate school for organic chemistry?
A. Yeah, I mean, I -- that's a functional group, and it's -- a nitrosamine, you have to have an amine, and it's -- so that's included in functional groups in organic chemistry.
Q. Right.
A. It's nothing that I worried about as a graduate student.
Q. Right. You would have to have --
A. It was just a functional group.

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Q. Sorry.
You would have to have an amine and a nitrosating agent under acidic conditions, right?
A. That's nothing that I studied in graduate school. I knew what a nitrosamine was. I didn't know how they formed or what reactions it would take.
Q. Do you know who Dr. Edwin Gump is at USP?
A. The name is not familiar. I've been gone for over 15 years, so he must be new or --
Q. If that --
A. -- since I left.
Q. Sorry.
Well, he's stated that nitrosamines can be formed, quote, Very simply through really simple chemistries.
Do you have any reason to disagree with that statement about how nitrosamines are formed?
MR. REEFER: Object to form.

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Beyond the scope.
THE WITNESS: I'd have to see what document -- what's his name, Gump, Dr. Gump that you're --
BY MR. DAVIS:
Q. Dr. Edwin Gump.
A. -- referring to? I'd want to try to see his documents and evaluate it for myself.
Q. Okay.
MR. DAVIS: Let's mark Tab 9, Jason, as Exhibit-4.
- - -
(Whereupon, Exhibit Sheinin-4, No Bates, USP Announces Approval of Chapter on Nitrosamines Impurities, was marked for identification.)
- - -
BY MR. DAVIS:
Q. And I apologize, Dr. Sheinin, it appears that when I printed this to PDF that part of the

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article's title was cut off.
It reads, USP Announces Approval of Chapter on Nitrosamines Impurities, dated December 3rd, 2021.
Do you see that?
A. Yes, I do.
Q. And then do -- you'll see in the third paragraph, there's a quote attributed to Edwin Gump, Ph.D., vice president of the Small Molecules Department at USP?
A. Yes.
Q. And he says that, One of the things that makes nitrosamines really tricky is that they actually can be formed very simply through really simple chemistries.
Do you see that?
A. Yes.
Q. You don't have any reason to -- you know, putting on your organic chemistry hat, do you disagree with that statement in any way?
MR. REEFER: Object to form.

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Beyond the scope.
THE WITNESS: His statement is nothing that I use in my report to offer my opinion in this case.
I'm not sure that it's really that simple. I would -- well, I'm going to leave it at that. It may be simple, it may not be quite so simple.
BY MR. DAVIS:
Q. And in writing your report in this case, did you refresh yourself on the chemistry by which nitrosamines are formed, specifically NDMA and NDEA?
A. I may have looked at whatever documents were provided and -- but I did not use any information as to how nitrosamines form, to form the basis for my opinion that's in my written report. It's not something that I was concerned with.
Q. Did you -- in preparing your report, did you look to see how NDEA specifically was formed in Mylan's

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valsartan API?
A. I did not specifically look to see how NDEA was formed in Mylan's product.
Q. Do you have -- do you have an idea of how NDEA was formed in Mylan's product?
MR. REEFER: Objection. Beyond the scope. Calls for speculation.
THE WITNESS: I'm not a process chemist, so I am not equipped to make a determination on how NDEA was formed.
And it just did not have any influence or input into the basis of my report. So it's beyond what I was asked to opine on.
BY MR. DAVIS:
Q. I think I know the answer to this question.
But you're not asserting any kind of opinion, one way or the other, regarding the genotoxic -- genotoxicity

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of NDMA or NDEA, are you?
A. I may be a lot of things, but I'm not a toxicologist. And the -- whether or not it's a potential genotoxic impurity or not is beyond my expertise.
Q. Are you familiar with -- and I think you have already mentioned it just in passing today, but you're familiar with ICH guidelines, correct?
A. I'm very familiar, well, with at least some of the ICH quality guidelines.
Q. Those would be the ones that are ICHQ? That start with ICHQ?
A. That's correct.
Q. Are you familiar with ICH M7?
A. I know what M7 is. I would not say that I'm really familiar with it.
Q. Did you look at it in preparing your expert report in this case?
A. I did not.
MR. DAVIS: Let me mark that

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as Tab 7 -- sorry, that's Tab 7, Jason. I'm going to mark that as Exhibit-5.
- - -
(Whereupon, Exhibit Sheinin-5, No Bates, M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Guidance for Industry, was marked for identification.)
- - -
BY MR. DAVIS:
Q. Do you have that in front of you, Dr. Sheinin?
A. Yes, I do.
Q. Okay. The title of -- the specific title of the guidance is, Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk.
Do you see that?
A. I see it.

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Q. If you'd flip to Page 5, Dr. Sheinin, there's a header titled, General Principles.
A. Okay.
Q. Take a few moments, if you would, to read that section, that's Subsection 3, General Principles, and it's on Page 5 and then goes down to the -- about the middle of Page 6.
And let me know when you're ready to discuss.
A. Okay.
Okay. I finished reading it.
Q. Let me start with a -- do you see that this guidance refers specifically to nitrosamines?
MR. REEFER: Object to form. Beyond the scope. Lack of foundation.
THE WITNESS: I see that it mentions N-nitroso compounds, among others.
BY MR. DAVIS:

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Q. And it refers to that group that includes N-nitroso compounds as the cohort of concern of high-potency mutagenic carcinogens.
Do you see that?
MR. REEFER: Object to form. Beyond the scope. Lack of foundation.
THE WITNESS: I see it, but it's not -- I'm not a toxicologist, so I can't evaluate how much the concern is. It's -- I can see the words on the paper, but I'm not in a position to be able to judge whether they're a risk or not.
BY MR. DAVIS:
Q. And I'm not asking you to, Dr. Sheinin.
The only purpose of this is I just want to ask you to confirm that, on its face, nitrosamines, N-nitroso compounds are subject to this guidance?
MR. REEFER: Object to form.

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Beyond the scope. Lack of foundation.
THE WITNESS: I'm not a toxicologist, but I can see the words on this paper -- on this page. It says, N-nitroso compounds.
BY MR. DAVIS:
Q. Right. And on its face, that means that N-nitroso compounds are subject to what's set forth in this ICH M7 guidance, correct?
MR. REEFER: Objection. Same objections.
THE WITNESS: I can see on this page that, yes, it says N-nitroso compounds. So N-nitroso compounds are included in this guidance.
But that's all I can say. I'm not in a position to be able to evaluate anything involved with N-nitroso compounds.
BY MR. DAVIS:

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Q. Right. But you would agree that this guidance does require manufacturers to do that evaluation, correct?
MR. REEFER: Object to form. Beyond the scope. Foundation.
Go ahead, if you know.
THE WITNESS: Again, I'm not a toxicologist, so what would need to be done in terms of N-nitroso compounds is beyond my expertise. And it does not form the basis for anything that's in my report.
BY MR. DAVIS:
Q. The title of the guidance is, Assessment and Control of DNA Reactive Impurities.
Do you have any opinion, one way or the other, as to whether Mylan appropriately assessed or controlled for potential nitrosamine impurities in its valsartan?
A. I'm not a toxicologist, so I really can't offer an opinion on whether

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Mylan did or did not do what you think that they should have done in terms of N-nitroso compounds. It's not anything that I used in my report, and it's beyond my expertise.
Q. Okay. You can put that away. We'll move on.
You mentioned at the FDA that you acquired a mass spec instrument in the early 1970s, right?
A. Yes.
Q. And then -- and then you coupled that with a gas chromatography system?
A. The instrument manufacturers, Varian, is the one who coupled it. It's nothing that I would be capable of doing.
But, yes, the company did couple the GC with the mass spectrometer.
Q. So were you telling me, then, that the FDA acquired a GC-MS that was coupled in the early '70s as well?
A. No. They -- we had gas

Page 89

chromatographs already. We bought the mass spectrometer. And I don't recall if it was a package to get the gas chromatograph, but I'm thinking we got the mass spectrometer first and then Varian came out with a mechanism to couple a gas chromatograph to a mass spectrometer.
And the mass spectrometer that we had operated in -- you had to have a vacuum, and trying to take the effluent from a gas chromatograph and putting it into a mass spectrometer was not something that we would have been able to do. And it was something that eventually the instrument manufacturers were able to do.
I don't believe that when we got our mass spectrometer initially that we had the capability to couple it to a gas chromatograph.
Q. But that was done a little bit later in the 1970s, it sounds like?
A. Yeah. Yeah.

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Q. Is the sensitivity -- was the sensitivity of the mass spectrometer back then substantially different from what it is today?
A. I don't know, but I would expect that advances have been made in mass spectrometry as well as in other types of detectors for gas chromatography.
It's just the nature of the advancement in science that sensitivity is always being improved.
Q. Well, at least one area that's developed is -- are you familiar with, like, predictive modeling, where you can run a chemical structure through a database and it will flag -- flag it as potentially mutagenic or genotoxic?
MR. REEFER: Object to form. Beyond the scope. Lack of foundation.
THE WITNESS: I'm not familiar with that type of database.

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BY MR. DAVIS:
Q. Okay. Have you ever heard of Derek Nexus?
A. I've heard of it. I'm not familiar with it.
Q. What about QSAR generally?
A. What about what?
Q. Quantitative structural-activity relationships, QSAR.
A. Oh. I've heard of it. I really don't know anything about it.
Again, I'm not a toxicologist, so I -- I've heard of it. I don't know how it works, and I don't know how to use it.
Q. You would agree, wouldn't you, that the GC and mass machines that have existed since they were coupled in the '70s, or even before then, that those were capable of detecting nitrosamines, correct?
MR. REEFER: Object to form. Beyond the scope. Incomplete hypothetical.

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THE WITNESS: I would have to know how much of any given ingredient or chemical we're talking about, in terms of whether it could be detected or not.
It would -- a lot would depend on what's in the column that's in your gas chromatograph, is it going to come off? It's very hypothetical, and I really can't give you an opinion one way or the other.
BY MR. DAVIS:
Q. That's not something you evaluated in this case, whether GC-MS machines were capable of identifying NDEA, NDMA in Mylan's valsartan in the quantities they were present therein?
MR. REEFER: Same objection.
THE WITNESS: That's correct, it's nothing that I used to form my opinions in my report.
MR. DAVIS: I'm going to mark Tab 11, Jason, as Exhibit-6.

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- - -
(Whereupon, Exhibit Sheinin-6, No Bates, Valsartan Guidance, was marked for identification.)
- - -
MR. REEFER: He has it, John. He's just reviewing it.
MR. DAVIS: Okay. Sure.
BY MR. DAVIS:
Q. Do you recognize this, Dr. Sheinin, as the 2020 version of the USP standard for valsartan?
A. I see that it's the monograph, official as of May 1st of 2020, USP, yes.
Q. Is this the USP that's currently effective?
A. I don't know if this is the one that's currently effective. I'd have to go online to the current -- to the USP online to see if there was a new version since May 1st of 2020. I can't say yes or no.

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Q. Do you see at the top there, there's an official status that says, Currently official on 28 January 2022?
A. Yes.
Q. Okay. Does that suggest to you that, at least as of that date, that that was the current USP monograph for valsartan?
A. Yes.
Q. Is there any place in this 2020 monograph that mentions anything about nitrosamines at all?
A. No.
Q. It's not your opinion, is it, then, Dr. Sheinin, that nitrosamines for this monograph only need to be controlled at not more than .1 percent, is it?
MR. REEFER: Objection to form. I think it's a double negative.
But go on, if you understood.
THE WITNESS: Can you repeat

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your question?
BY MR. DAVIS:
Q. Okay. It's not your opinion, is it, Dr. Sheinin, that nitrosamines only need to be controlled at point -- not more than .1 percent, is it?
MR. REEFER: Object to form. Do you mean per the monograph or in general?
MR. DAVIS: I'm asking -- I'm asking him generally.
BY MR. DAVIS:
Q. My question is, you've told me that nitrosamines aren't mentioned anywhere in this monograph.
My question is, does that mean, in your opinion, Dr. Sheinin, that nitrosamines only need to be controlled at not more than .1 percent, as stated in this impurity section on the USP monograph?
A. It's not something that I feel I can address, because I'm not a

Page 96

toxicologist and I don't know at what level those nitrosamines would have to be controlled.
Q. They would be -- in other words, what you're telling -- let me crystallize what you're telling me.
I think what you're telling me is that, aside from this USP monograph, there would be other -- other regulatory items, so to speak, that would set different limits for nitrosamines, correct?
A. There's always requirements in an NDA or an ANDA application, in the specification, that has tests that are not included in the USP monograph. So it's entirely possible that there could be additional information in what's filed at FDA than what's in a USP monograph.
Q. Right. And, I guess, just to tag a general point on that, the USP monograph is not the end-all, be-all in terms of tests that are required to be done on a -- in this case, an API for

Page 97

valsartan, or another substance, correct?
MR. REEFER: Object to form. Go ahead.
THE WITNESS: According to the Food, Drug and -- Federal Food, Drug and Cosmetic Act, a drug product or a drug substance or an API, if you will, if there is a USP monograph, that material has to meet the requirements in a USP -- in the USP monograph.
FDA has the authority to ask for additional requirements in the specification that's approved generally. Companies include tests and procedures in their drug application that are not included in the USP monograph.
BY MR. DAVIS:
Q. Right. There are additional tests and limits that can apply that just simply aren't in the USP monograph, correct?
A. Yes, there are -- there are

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tests and procedures and acceptance criteria in the specification that's included in an approved application that are not in the USP.

Q. And in the case of N-nitroso compounds specifically, we just saw ICH M7, which provides some guidance on testing and limits to control for nitrosamine impurities specifically per that guidance, right?

MR. REEFER: Object to form. Beyond the scope. Lack of foundation.

THE WITNESS: I saw what was on -- whatever -- the Page 5 of that guidance, that it mentioned N-nitroso compounds.

BY MR. DAVIS:

Q. You list a number of Mylan fact witness depositions in your Exhibit B to your report.

Do you recall listing those?

A. I recall that they are on the list and they are things that counsel

Page 99

provided to me.

Q. Did you ask counsel if that was all of the Mylan fact witness depositions that have been taken in the case?

A. I did not.

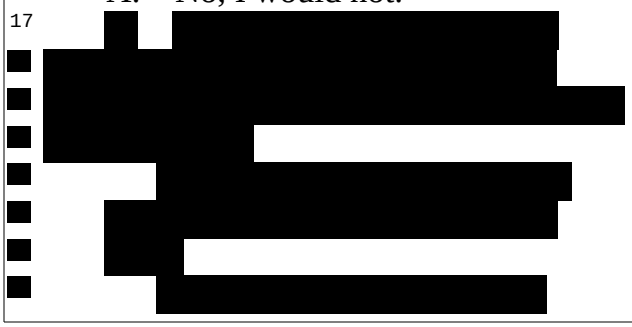
Q. You don't list the deposition of Wayne Talton.

Is there -- did you know that he was deposed in this case?

A. The name is not familiar to me.

Q. You wouldn't know him as Mylan's regulatory affairs corporate witness in this case?

A. No, I would not.



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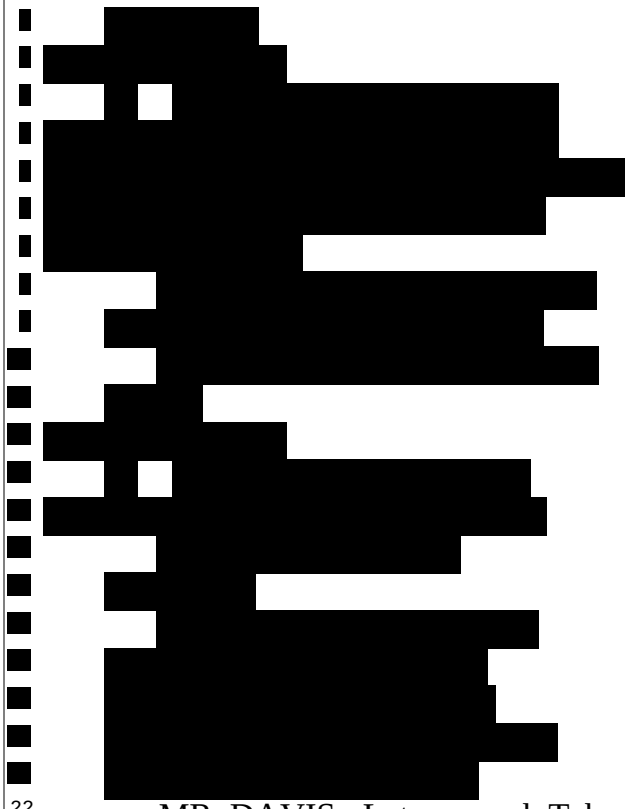

MR. DAVIS: Let me mark Tab 12, Jason. That will be Exhibit-7.

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- - -

(Whereupon, Exhibit Sheinin-7, MYLAN-MDL2875-00705126, 3/14/19 Cover Letter for Master File GDUFA Complete Response Letter, was marked for identification.)

- - -

MR. REEFER: This is being marked as 7, right, John?

MR. DAVIS: That's correct, Exhibit-7.

MR. REEFER: Okay. I'm just making sure I was keeping count.

BY MR. DAVIS:

Q. Dr. Sheinin, you'll see there's a yellow exhibit sticker -- or maybe it's not yellow if it printed in black-and-white, but there's a sticker on the first page that says Exhibit Plaintiff Talton-11.

Do you see that on the top right corner of the very first page of the document?

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A. Yeah.
PL-Talton-11?
Q. Right.
A. Yes, I see it.
Q. And you'll see that the --
yes.
And you'll see that the file name on that page of the file, as it was produced to us by Mylan, says, DMF Quality Information Amendment 20190314?
A. Yes.
Q. Okay. If you go to the fourth page of the document, you'll see a header, valsartan DMF Number 018253. And then, Response to valsartan DMF letter, dated February 5th, 2019.
Do you see that?
A. Yes.

[redacted]

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[redacted]

Page 104

[redacted]

Page 105

[redacted]

Page 106

[redacted]

BY MR. DAVIS:

Q. Right. And that's because

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counsel didn't provide you Mr. Talton's testimony and this exhibit, correct?

MR. REEFER: Object to form. Argumentative. Beyond the scope. Foundation.

THE WITNESS: I have not seen this document before. So, yes, I did not receive it. I've not seen it.

BY MR. DAVIS:

[redacted]

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[redacted]

BY MR. DAVIS:

Q. Turning to your report for a second, Dr. Sheinin, in Paragraphs 64 to 66 -- and I'm going to paraphrase you here, and feel free to take issue with my paraphrasing if you'd like, but --

A. Which paragraphs again?

Q. Sure. Paragraphs 64 through 68, under the header, Mylan's Valsartan API Manufactured Between Market Entry in 2012 and the Recalls in 2018 Complied With the Standards and Specifications in Place at the Time of Manufacture.

A. Yes.

Q. You write there in that section -- or one of the things you write is that the valsartan USP monograph did not contain any testing or acceptance

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criteria for nitrosamine content.

And I'm specifically guiding you to Paragraph 66.

Do you see that?

A. Yes.

Q. Why is that relevant to you? What's the point of having that in your report?

A. The relevance is that I'm opining on the fact that Mylan's valsartan API, manufactured between market entry in 2012 and the recalls in 2018, complied with the standards and specifications in place at the time of the manufacture.

So it's relevant in that there was no mention in the USP monograph of the need to test for nitrosamines.

Q. Okay. But that doesn't mean that Mylan's valsartan was okay simply because it met the USP monograph, correct?

MR. REEFER: Object to form. Vague.

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THE WITNESS: It meant that the -- Mylan's valsartan met the USP monograph prior to recalls of 2018, and Mylan's valsartan products are on the market today. They meet the USP monograph. They meet the specifications in the FDA-approved applications. They have USP on the label of the -- both the drug product, valsartan tablets USP, and they also include the USP on the drug substance, valsartan USP.

So at this point I've lost track of what your initial question was.

BY MR. DAVIS:

Q. Well, sure, let me -- let me ask it this way.

Is it your testimony, Dr. Sheinin, that between Mylan's entry on the market in 2012 and the time of recall in late 2018/early 2019, that nitrosamines only had to be controlled at

Page 111

not more than .1 percent per the USP monograph?

A. The monograph, as well as the specification in the approved application, includes, in the impurities section, a requirement for any unknown impurity not more than 0.1 percent.

So in order to meet the requirements of the USP monograph and the ANDA specification for the API, any other unknown impurity would need to be controlled to not more than 0.1 percent.

Q. So it is your opinion, then, that during that timeframe Mylan only had to control nitrosamine impurities at not more than .1 percent?

Are you saying that the USP standard governs solely Mylan's marketability of its products?

A. I'm not equipped to discuss the marketability of a product. I'm a chemist, that's not my area.

But in order for Mylan to be on the market, they have to meet the USP

Page 112

monograph and they have to meet the specification requirements in the approved application.

Q. And the approved application here is the ANDA, correct?

A. Correct.

Q. And that references the DMF in this case by Mylan, which you said you didn't review, correct?

A. Correct. Because drug master files are not approved or not -- and not not approved.

Q. Well, in this case, Mylan -- Mylan's ANDA referenced the drug master file, so it became incorporated into the ANDA.

Do you understand that?

A. That's correct. And that's -- that's the way it works.

But DMFs by themselves are not approved or not -- and not not approved. The FDA takes no -- no regulatory action on drug master files.

Q. Right. But they would have

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taken an action on the ANDA in this case, which incorporated, by reference, the drug master file, correct?

A. Yeah. As I believe is included in my -- in my expert report, that when there's deficiencies in a drug master file, the NDA or ANDA holder -- or it's possible to have a DMF that references another DMF.

So however it works, the FDA would say in a letter to the applicant that there's issues or deficiencies in the drug master file, and the FDA would send a detailed letter to the drug master file holder detailing what those deficiencies or issues are. But they would not communicate to the NDA or ANDA applicant what those deficiencies are.

And I think that's included in my report. So that's how that works.

Q. Well, sure. But what I was asking was whether the -- in the setup that Mylan had, where they chose to submit an ANDA and then incorporate, by

Page 114

reference, their drug master file, that's submitted with the ANDA to the FDA, correct, and reviewed by the FDA as part of the ANDA review process, is it not?

A. I don't think that's exactly right.

The drug master file is submitted separately to the agency, and there's a letter authorizing reference to the drug master file that's included in the ANDA. But the ANDA and the drug master file are not submitted at the same time to the same place.

Q. Okay. Well, taking that, that they can come in waves -- I take your point there.

The point -- the point I'm trying to make, though, is that when the ANDA is submitted -- let's say the drug master file is submitted a month beforehand. When the ANDA is submitted, that makes reference and incorporates by reference the drug master file, that becomes, essentially, part of the ANDA

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submission that the FDA reviews in determining whether to approve the ANDA, correct?

A. I wouldn't say -- well, from a -- I'm not a lawyer, so I can't say how that's incorporated -- a drug master file is incorporated into the application.

But the drug master file may or may not be reviewed for a given ANDA. It depends on whether the drug master file has been reviewed in the past and found to be acceptable. So when a new ANDA comes in, that drug master file may or may not be reviewed. It depends --

Q. Well, let's -- well, let's take Mylan's first ANDA here that was approved. There were three ANDAs.

You're familiar with that, right?

A. Yes.

[redacted]

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[redacted]

Q. Okay. And you just told me you haven't reviewed the ANDAs in any particular detail and you haven't reviewed the DMF at all, correct?

A. Correct.

Q. Let's say, Dr. Sheinin, that there was a discrepancy between the impurity limits in the USP monograph and the limits approved or set by the FDA, whether approving an ANDA or in some other guidance document or official FDA document that sets limits, which would

Page 117

control in that instance? Would the USP monograph limit control or would the FDA approved limit control?

A. If I remember correctly, the USP acceptance criteria would control. But I'm not 100 percent certain of that.

MR. DAVIS: I'm going to mark Tab 10, Jason, as Exhibit-8.

- - -

(Whereupon, Exhibit Sheinin-8, No Bates, Impurities in Drug Products and Drug Substances - A USP Approach, was marked for identification.)

- - -

BY MR. DAVIS:

Q. Do you have this set of USP slides in front of you, Dr. Sheinin?

A. I do.

Q. Do you see that it's titled, Impurities in Drug Products and Drug Substances - A USP Approach?

A. Yes.

Q. Do you know who

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Dr. Ravichandran is?
A. I do. I hired him.
Q. Have you seen this presentation before?
A. I don't believe I have.
Do you know where it was given?
Q. You might see in very, very grayed-out text on the first page that says, Last update, March 2018.
Do you see that?
A. On the first page here of the exhibit? I don't see anything about that.
Q. Okay. It might be too grayed out in the way it printed.
I'll represent to you that the document --
A. Oh, yeah. It's very, very light. I can't -- I can't see that.
Q. And then even smaller text on the bottom right corner of each page, also grayed out, is a, Copyright 2020, USP.

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Do you see that?
A. I see something. I can't tell you what it says.
Q. Okay. Do you hold Dr. Ravichandran in high regard?
MR. REEFER: Object to form.
THE WITNESS: Yes.
BY MR. DAVIS:
Q. You think he's quite knowledgeable?
MR. REEFER: Object to form. Vague.
THE WITNESS: I think he's knowledgeable. I don't know that he's more or less knowledgeable than other scientists at USP.
BY MR. DAVIS:
Q. Do you think he's quite knowledgeable regarding the USP approach to impurities and drug products and drug substances, which is the title of this presentation?
MR. REEFER: Object to form. Vague. Foundation.

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THE WITNESS: I think he's knowledgeable to the point that his supervisor approved giving this presentation.
Again, I can't say that he's more or less knowledgeable about the topic than other scientists at USP. It's -- I -- there's only a handful of USP scientists who are still there from when I left.
BY MR. DAVIS:
Q. Flip to Page 9 as it's numbered on these slides.
And it's, again, in very small numbering, gray text in the bottom right corner. You'll see a slide that's titled, Contents.
MR. REEFER: John, if you're going to ask questions about, you know, the substance of this, can we have an opportunity to go through it? I think Dr. Sheinin said he had not seen the presentation before.

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MR. DAVIS: I mean, sure. It's 90 pages, Jason, and I only have questions regarding, at most, a couple of them. So I'm not sure --
MR. REEFER: All right.
MR. DAVIS: -- if fully reviewing the document in different aspects of it will pertain to what I want to talk about.
I mean, what if we -- what if we did this, I'll ask my questions, and if Dr. Sheinin wants to review the pages surrounding that for context, I'm happy to let him do that.
MR. REEFER: Yeah. John, I'm not trying to interrupt you. I just want to give him a fair opportunity based on his testimony he hadn't seen it before.
So if the doctor says that, you know, he needs to take a

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minute to understand it, I just ask that you let him do so. That's all.

Fair enough?

MR. DAVIS: Fair enough.

MR. REEFER: Cool. Thank you.

BY MR. DAVIS:

Q. So you're at Page 9, the table of contents for this presentation, Dr. Sheinin?

A. I see on Page 3 of what you've given me something that says, Contents. I don't know what's -- I can't see any page numbers.

Q. Yes. Is it -- did it print out for you as four slides to a page?

A. Two slides to a page.

Q. Two slides to a page.

A. Yes.

Q. Okay. I see.

So the contents section actually appears twice, it appears. So we can -- we can stick on the one you're

Page 123

on.

And, I guess, do you see where it says -- there's a header, Guidelines, guidances? And it says, ICH FDA, below that?

A. Yes.

Q. Why would -- why would Dr. Ravichandran include ICH/FDA guidelines and guidances in a presentation that's titled, A USP Approach to Impurities?

MR. REEFER: Object to form. Foundation. Calls for speculation.

THE WITNESS: I don't know why he included them. I'd have to ask him why he included this as a topic.

BY MR. DAVIS:

Q. Why would they be --

A. I'm not --

Q. Why would they be --

A. I'm not in a position --

MR. REEFER: Can you let him

Page 124

finish, John? Sorry about that.

MR. DAVIS: Yes, go ahead.

THE WITNESS: I'm not in a position to be able to say why he included them. I don't know.

BY MR. DAVIS:

Q. Why would -- let me ask it this way, then: Why would ICH/FDA guidelines and guidances be germane to discussing in a presentation titled, A USP Approach to Impurities?

MR. REEFER: Object to form. Foundation. Calls for speculation.

THE WITNESS: I can't tell you exactly why. I can tell you that there were times when ICH created a guidance, in FDA perspective, in ICH perspective, when they created a guideline where USP eventually modified a general chapter to be in agreement with what ICH did.

So that's the only reason I

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might be able to offer. But I don't know -- I don't know what was in Ravi's mind as to why he included them in this presentation. It's beyond my capability to tell you why.

BY MR. DAVIS:

Q. Okay. Turn, if you would, to the slide that's numbered 36.

A. What's the -- I don't see any numbers on any of them, so what's the heading?

Q. Okay. Flip until you find a USP sort of face page that says, Discussion, in bold lettering. It should be about 15 or so pages in.

A. I see something that says Discussion and contents listed again.

Q. Yes, correct.

And then if you flip a few pages further than that, you'll see a question and answer.

The question is, If a manufacturer controls impurities and

Page 126

degradation products in accordance with only a pharmacopeial monograph, is that acceptable to the regulators?

Do you see that?

A. No.

Q. It should be four -- the fifth slide after that discussion face page.

A. So if we're counting slides --

MR. REEFER: John, would you mind if I went over and helped a little bit?

MR. DAVIS: Sure. If you know where it is, Jason, feel free to show it to him.

MR. REEFER: I think the challenge we're facing is the way it's printed, the slide number is super-duper faint.

And so if you don't mind, I'm going to stand up and just walk around the table.

MR. DAVIS: Okay. Not a

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problem.

THE WITNESS: Maybe I had the wrong discussion slide.

MR. REEFER: I think there's a -- I think there's a number of instances where the heading, Discussion, appears, and I think you guys might have landed on different pages.

But, ultimately, Mr. Davis will confirm. But the top of the slide that I'm looking at, John, says, Source of impurities, and it's got a little demonstrative. And then below that it's the second slide that begins with question.

MR. DAVIS: Yes, that's right.

Thanks, Jason.

MR. REEFER: You're welcome.

BY MR. DAVIS:

Q. Okay. So you'll see the question presented there is, If a

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manufacturer controls impurities and degradation products in accordance with only a pharmacopeial monograph, is that acceptable to the regulators?

Do you see that?

A. I see it.

Q. And then Ravi responds to that question by saying, in the second bullet point of his answer, that, A particular manufacturer's manufacturing method for formulation components may lead to unexpected impurities due to a different route of synthesis, different reagents, et cetera. Different processes may lead to different impurities.

Do you see that?

A. Yes.

Q. And then -- then he continues in the third bullet, it says, If an individual monograph is inadequate to control an impurity, the manufacturer is responsible for developing and validating appropriate analytical procedures, establishing acceptance

Page 129

criteria, and communicating with USP.

Do you see that?

A. Yes.

Q. Okay. At any time between 2012 and '18, did you see any evidence that Mylan had attempted to communicate with USP regarding setting an acceptance criteria and test for NDMA or NDEA?

A. I did not see anything that -- of that nature.

MR. REEFER: Object to form and scope.

But go ahead.

BY MR. DAVIS:

Q. Do you disagree with the way that Ravi has answered the question as presented?

MR. REEFER: Object to form and scope.

THE WITNESS: This is -- this is why, when I was at USP, we developed the flexible monograph approach. Because if the innovator either synthesizes their

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API themselves or purchases it from a third party and an ANDA comes along and a generic company purchases the active ingredient from a different source that's using a different manufacturing procedure, they almost certainly will introduce a different set of impurities; some may be the same as in the innovator's product, some may be different.

And USP created this flexible monograph approach between Roger Williams and myself and another chemist who worked for me. And we have a procedure where a company, as it says here, if the individual monograph is inadequate to control the impurity, the manufacturer is responsible for developing, validating appropriate analytical procedures and communicating with USP.

So that's a way for the

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generic to meet the USP monograph, even if they have a different set of impurities.

And the way that works, then, if there would be more than one impurity procedure, as I mention in my report, that I don't -- I'm not sure that I mentioned this part in the report, but if you're using Impurity Procedure 1, you don't have to say anything. If you're using Impurity Procedure 2, you would have to say something in your labeling. And I give an example in my report to that extent.

So that's -- that's the premise for why we developed this flexible monograph approach.

BY MR. DAVIS:

Q. So what Ravi is essentially describing here in his answer is the flexible monograph approach, correct?

A. Essentially, yes.

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Q. Do you agree that manufacturers are responsible for evaluating their manufacturing method for these different impurities that may result from that specific method that they're undertaking?

MR. REEFER: Object to form. Scope.

THE WITNESS: I would agree that manufacturers are responsible for the analytical methods that are used to control impurities in their drug substance and drug product, if that's what you're asking.

BY MR. DAVIS:

Q. Right. They're responsible for evaluating their manufacturing method for potentially different impurities and then if they -- if they find them or are -- let me strike that.

Manufacturers are responsible for both evaluating their manufacturing method for these different

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impurities, like Ravi mentions, and then once identified, they are also responsible for developing controls for them, which is what Ravi describes in the third bullet of his answer, correct?

MR. REEFER: Object to form. Scope.

You can answer.

THE WITNESS: Companies are responsible for developing the analytical methods and validating them to control whatever impurities are found in their drug substance or in their drug product.

BY MR. DAVIS:

Q. Well, they're not -- would you agree, manufacturers aren't just responsible for controlling for impurities they happen to find in their drug substances or products, they're also responsible for evaluating the process chemistry to predict potential impurities that may arise from the chemical

reactions that take place, right?
MR. REEFER: Object to form. Beyond the scope.
THE WITNESS: That's a position or a responsibility for a process chemist who is designing the process. That's not something that I'm familiar with doing.
BY MR. DAVIS:
Q. But you're --
A. I can't agree or disagree with you.
Q. Okay.
MR. DAVIS: Let me mark Tab 13, Jason.
MR. REEFER: Can we put the slides away, John, the USP stuff?
MR. DAVIS: Yes, for now.
MR. REEFER: Okay. That was ominous.
THE WITNESS: Can we go off the record for a second?
MR. DAVIS: Sure. Yes.
MR. REEFER: I'm sorry,

before we do, John, can you just say again what you want me to get?
MR. DAVIS: Yes. Tab 13.
MR. REEFER: Tab 13?
MR. DAVIS: Yes. I'm marking it as Exhibit-9, before we go off the record.
- - -
(Whereupon, Exhibit Sheinin-9, No Bates, FAQs: Organic Impurities, was marked for identification.)
- - -
MR. DAVIS: Okay. We can go off.
VIDEO TECHNICIAN: Going off the record. The time is 12:37 p.m.
- - -
(Whereupon, a discussion off the record occurred.)
- - -
VIDEO TECHNICIAN: We are back on the record. The time is

12:38 p.m.
BY MR. DAVIS:
Q. Okay. Do you have what's been marked as Exhibit-9 in front of you, Dr. Sheinin?
A. Yes, Tab 13. I'm trying to write down the numbers. That's 9.
Okay. Yes, I have it.
Q. You'll see that it's an FAQ document, FAQs: Organic impurities.
Do you see that?
A. I see that. I see also it's a -- something from USP.
Q. Correct. It's been pulled from the USP website. The URL is at the bottom, https://www.usp.org, frequently asked questions, organic impurities.
Do you see that?
A. Yes.
Q. And one of the FAQs at the bottom, specifically the fourth one at the bottom of Page 1, is, What does it mean to characterize the impurity profile of a product?

Do you see that?
A. Yes.
Q. And then there's an answer that appears on Page 2 of 3, correct?
A. Where is the answer?
Q. The answer appears on the next page. It starts with, As described in applicable guidance.
Do you see that?
A. Oh, so this is -- this is answering all four of these questions in one --
Q. No, no. What I've done -- I'll explain --
MR. REEFER: It looks like it's probably a drop-down, Dr. Sheinin, so.
MR. DAVIS: That's correct.
MR. REEFER: If you just click on --
MR. DAVIS: He's right.
BY MR. DAVIS:
Q. It's a drop-down. And to make the document less lengthy, I've only

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dropped down the question that I'm interested in seeing the answer to.

A. Oh, okay.

MR. REEFER: Then I'll object on the basis that we don't have the complete document before us.

But with that said, if you want to ask questions about it, go ahead.

MR. DAVIS: Sure.

BY MR. DAVIS:

Q. So do you see where the answer to that question, What does it mean to characterize the impurity profile of a product, starts on Page -- the next page?

A. I'd like to read it. I'd like to --

Q. Sure. Take a moment to read it.

A. -- be able to read it.

Okay.

Q. Okay. Have you had a chance

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to read the answer that USP provides to that question?

A. Yes.

Q. And it starts with -- it starts with, As described in the -- sorry. What was that, Dr. Sheinin?

A. I was going to say, are these next bullets, are they part of the answer? Or are they --

Q. No, those are additional frequently asked questions regarding organic impurities that come up.

So what I'm directing your attention to --

A. Okay.

Q. -- is the question and answer that I read out for you, which is, What does it mean to characterize the impurity profile of a product? And then the answer that USP provides.

Do you understand that?

A. Yes.

Q. Okay. And the first part of the answer starts with, As described in

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applicable guidance, which include but are not limited to -- and then it refers to some of the ICHQ guidances.

Do you see that?

A. Yes.

MR. REEFER: Objecting to the form. Beyond the scope. But, go ahead. Sorry.

BY MR. DAVIS:

Q. So would you agree that even if there is a USP monograph for a product, that doesn't mean that the manufacturer doesn't also have to comply with other applicable guidance, for example, such as ICH guidances as the USP states here, correct, especially regarding organic impurities, right?

MR. REEFER: Object to form. Beyond the scope.

Go ahead, Dr. Sheinin.

THE WITNESS: I believe USP is in agreement with the ICH guidances, in terms of how impurities are handled in their

Page 141

monographs. So there's -- they are in agreement.

BY MR. DAVIS:

Q. Well, my question, and maybe you're answering it in an indirect way, but my question is, even if there is a USP monograph for a product, that doesn't mean that any other applicable guidances, as USP terms it here, including, specifically, ICH guidances, that those aren't -- that those aren't likewise applicable even in the presence of a USP monograph?

MR. REEFER: Same objection.

Go ahead, Doctor.

THE WITNESS: FDA -- FDA says guidances are suggestions. So I -- there are other approaches that a company can take that could differ from an ICH guidance, as well as an FDA guidance.

So I can't say that companies are required to follow other guidances. They are not

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required to. They can have different approaches.
BY MR. DAVIS:
Q. If a company were to take a different approach under an ICH guidance, isn't that something they would have to consult with the FDA about first?
MR. REEFER: Objection. Beyond the scope.
THE WITNESS: FDA's guidances -- ICH guidances, in and of themselves, don't have anything to do with FDA, sort of. FDA has to publish those guidances before they become FDA official guidances.
But once they -- once they publish them, there's no difference between an ICH guidance and an FDA guidance. They're one and the same. So I can't distinguish an FDA guidance from an ICH guidance.
BY MR. DAVIS:

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Q. My general question, though, is, even where a USP monograph exists, there are other applicable guidances, regulations, et cetera, that don't just go away, right?
MR. REEFER: Object to form. Beyond the scope.
THE WITNESS: I don't -- I don't discuss these other ICH guidances or other FDA guidances to form the basis of my opinion in my report. So I'm -- I'm at a loss to understand what you're really asking me.
BY MR. DAVIS:
Q. Well, what I'm asking you, and I'll phrase it differently, but just because, you know, you haven't talked about it in your report doesn't mean I'm not entitled to ask you a question about it.
My -- let me ask it this way: When there's a USP monograph, the USP monograph doesn't just supercede

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other applicable FDA guidances, regulations or other FDA authorities that exist, right?
A. As a layperson, not a lawyer, I can't really comment on the legal aspects of that. So it's difficult for me to give you an answer to that. From a legal perspective, it's out of my area.
Q. So you're not holding yourself out as a regulatory expert?
A. I'm not holding myself out as a legal expert.
Q. Well, my question is a regulatory one, not a legal one.
My question is, when there is a USP monograph for a product, does that supercede and just make, you know, irrelevant other -- other applicable regulations or guidances, including, for example, ICH guidances that the FDA has adopted?
A. I think I said earlier that USP in general is in conformance with ICH

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guidances. So I don't know that there's a difference there.
MR. REEFER: John, if you're happening to transition, do you want to talk a little bit about planning? We've been on about an hour and 50 minutes here.
MR. DAVIS: Let me just finish this document, and then we can talk about that.
BY MR. DAVIS:
Q. If you look at the next paragraph, Dr. Sheinin, it says, The methods used to characterize an impurity profile include, but are not limited to, a sound scientific appraisal of the chemical reactions involved in the synthesis of the drug substance and the impurities associated with raw materials, et cetera, et cetera.
Do you see that?
A. Yes.
Q. That's consistent with what Ravi is saying in his presentation we

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looked at in Exhibit-8, right, that you can't just rely on a USP monograph, you have to do a sound scientific appraisal of your own manufacturing method, right?

MR. REEFER: Object to form. Asked and answered.

THE WITNESS: The -- whoever is developing the process to create the drug substance is a process chemist, and they would be the ones to understand that process.

It's not something that I feel comfortable or capable of second-guessing what a process chemist would do. It's not something that I have done, as I have not worked in the industry, and it's not something I've done where you have to scale up a process. It's just not within my expertise.

BY MR. DAVIS:

Q. And I'm not -- I'm not

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asking you, Dr. Sheinin, to comment on the substance of any particular scientific appraisal of impurities that was done by anyone, including Mylan.

I'm just asking you to confirm what USP is saying here and what Ravi said in his presentation we just looked at in Exhibit-8, that such an obligation exists?

MR. REEFER: Object to the form. Scope.

THE WITNESS: And I think I discussed before about the purpose of an analytical method is to detect and quantify, or in some cases to qualify, impurities in these materials.

So I would have to say that there needs to be analytical procedures to control impurities in drug substances and drug products.

BY MR. DAVIS:

Q. Not just analytical

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procedures, though; there actually has to be -- and I hear you when you say this is a process chemist's job to do substantively, but there has -- there has to be an evaluation, i.e., what -- in the USP's terms, a quote, sound scientific appraisal of the chemical reactions.

Do you disagree that that's what the -- do you disagree with this USP document here, that that obligation exists?

MR. REEFER: Object to form. Scope.

But go ahead, Doctor, you can answer.

THE WITNESS: I'm rereading this paragraph.

I have difficulty in putting into general terms this. Yes, I think you need to be able to look at your analytical method and have a technique, whatever your detection is, to be able to identify whatever impurities are

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in the -- whatever analyte you're looking for.

BY MR. DAVIS:

Q. Okay. But that's analytical chemistry.

What --

A. That -- that's what I can talk to.

Q. Okay. So you have no opinion on whether a manufacturer is required to do a sound scientific appraisal of the chemical reactions involved in its manufacturing process?

A. I did not use anything in this -- that's discussed in this document to form the basis of my opinions about USP.

As I mention, I did talk about the flexible monograph approach, and I understand that different routes of synthesis can lead to different impurities. And that's a way for USP to be able to have companies able to meet the requirements of the monograph, even

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when the impurity profile is different than what is there in the -- from the innovator product.

Q. And as part of that flexible monograph approach, that requires somebody to look at how -- how their method of manufacture may differ from another method and to predict the kinds of impurities that may arise from that -- from that -- those changes in the manufacturing method, correct?

That's part of the sound scientific appraisal that the USP is referring to here, is it not?

MR. REEFER: Object to form. Scope.

Go ahead, Doctor, you can answer.

THE WITNESS: I'll have to fall back on what I've said. There has -- the method that's used is different depending on what the impurity profile is.

So there's a -- that's why

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USP created the flexible monograph approach.

BY MR. DAVIS:

Q. Are you familiar with FDA guidances on conducting risk assessments?

A. On what?

Q. Conducting risk assessments?

A. For nitrosamines or just in general?

Q. No, generally.

A. No, I'm not.

Q. Okay. And in working on your report, did you see any evidence that Mylan had done a sound scientific appraisal of the chemical reactions involved in the synthesis of Mylan's valsartan API for impurities?

MR. REEFER: Objection to form. I'm sorry, John. I thought you were done. I apologize.

Objection to form. Beyond the scope. Asked and answered.

THE WITNESS: I did not look to see if there was anything as

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you described. I did not go through the drug master file, which is where any information like that would have -- would have been.

There was really nothing in the application, in the ANDA that I looked at, that contained any information of that type. I did not see anything. I have no way of knowing if it's there or not.

BY MR. DAVIS:

Q. Let's say that someone did do a sound scientific appraisal and it led them to believe they might be creating nitrosamine by-products in their drug substance.

Are you with me?

MR. REEFER: What's that, John? You broke up.

MR. DAVIS: Sure.

BY MR. DAVIS:

Q. I'm asking you a hypothetical, Dr. Sheinin.

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The hypothetical is, let's say there was someone at a generic manufacturer who did a sound scientific appraisal of the chemical reactions for an API drug product substance and believed, as a result of that sound scientific appraisal, that the process would create nitrosamine by-products.

Do you follow me?

A. I follow you.

Q. What would be their obligation under applicable guidances and regulations to do next, do you know?

MR. REEFER: Objection to form. Incomplete hypothetical. Beyond the scope. And foundation.

But go ahead.

THE WITNESS: I'm not prepared to answer hypothetical questions. It's --

BY MR. DAVIS:

Q. There's no basis for you not to answer any question.

MR. REEFER: John, you

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interrupted him.
MR. DAVIS: Well, look, he's saying he's not willing to answer a hypothetical question. That's not how this works. I'm entitled --
MR. REEFER: He wasn't --
MR. DAVIS: -- to ask questions --
MR. REEFER: He wasn't -- John, he wasn't even able to finish his answer. So I think it's a little bit presumptuous to suggest how he was going to respond in totality. Perhaps --
BY MR. DAVIS:
Q. You followed --
MR. REEFER: -- you should let him respond.
BY MR. DAVIS:
Q. You followed my hypothetical question.
What's your answer to it, Dr. Sheinin?

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MR. REEFER: Object to form. Incomplete hypothetical. Beyond the scope. And foundation.
But go ahead, Doctor, you can continue your answer.
THE WITNESS: I would have to have some data, I would have to have some real information to be able to address a hypothetical question.
It depends. It could be yes, it could be no. It's just -- it's hypothetical. It's not real world.
BY MR. DAVIS:
Q. No. I respectfully and wholeheartedly disagree.
I'm asking you, not quantitatively, I'm asking you qualitatively, if a person at a pharmaceutical manufacturer did a sound scientific appraisal and said, oh, we might be creating nitrosamine by-products, what's their obligation,

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under the regulations, to do next, do you know?
MR. REEFER: Object -- objection to form. Beyond the scope. Incomplete hypothetical. And foundation.
Go ahead, Doctor, if you know.
THE WITNESS: I don't know what the obligation is under applicable guidance. I -- I have to go back and reread some of those guidances to see if there is language to that effect that says exactly what you said.
BY MR. DAVIS:
Q. Would it be your expectation -- and I get that you haven't actually reviewed the necessary documents in this case.
But would it be your expectation that Mylan, here, did a sound scientific appraisal for potential genotoxic impurities, based on its

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detailed laboratory process for creating valsartan API?
MR. REEFER: Object to form. Beyond the scope.
You almost acknowledge this is beyond the scope, John. I mean, you keep asking these questions. But, you know, at some point there's got to be some connection to the report, right?
But with that being said, go ahead, Doctor, if you can --
MR. DAVIS: Let me respond to that briefly, Jason. I'm entitled to ask him about what's in his report. I'm also entitled to point out things that he hasn't looked at, at all, or that he might -- he might think relevant or that he might, if he hasn't reviewed them, might -- you know, this is in his wheelhouse.
So, you know, I'm entitled to ask the question even if it's

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not in the report, because it's part of his -- his 40 years of work at the regulator and at USP, and it's tangential to what he's got in his report.

So, yeah, I'm entitled to ask the question.

MR. REEFER: Well, that's incorrect, John. You can't force him to offer opinions that he hasn't formulated for purposes of this litigation on the spot, on the fly, based on your hypotheticals.

He says that he hasn't done this analysis. He's not offering the opinion on whether Mylan's DMF was adequate or otherwise.

BY MR. DAVIS:

Q. Would you expect that it was adequate, given what you know about the facts of this case?

MR. REEFER: Objection to form. Foundation. Scope.

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Go ahead.

BY MR. DAVIS:

Q. Would you expect, Dr. Sheinin, that Mylan did, in fact, do a sound scientific appraisal for potential genotoxic impurities, based on its detailed laboratory process, when, in fact, there were genotoxic impurities in Mylan's valsartan?

Would you expect --

MR. REEFER: Object to form.

BY MR. DAVIS:

Q. -- they did do that, given what the history showed?

MR. REEFER: Object to form. It's compound. Beyond the scope. Lack of foundation. Incomplete hypothetical.

But go ahead, Doctor.

THE WITNESS: The fact that Mylan is on the market and FDA has not, again, recalled or asked Mylan to recall their product says to me that their DMF is adequate

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and FDA has no reason to take other regulatory action.

BY MR. DAVIS:

Q. Are you -- sir, are you not aware that Mylan recalled every single lot and batch of valsartan API that was on the market in 2018 and 2019? Are you not aware of that fact?

A. I'm aware of that. I'm also aware that Mylan is back on the market.

Q. Okay. But you haven't -- we've gone over this about four or five times today.

You have no idea the circumstances how they got back on the market, do you?

MR. REEFER: Object to form. Argumentative. Beyond the scope.

MR. DAVIS: Well, he says it's not in his report, and yet he keeps bringing up the fact that Mylan is back on the market, and he doesn't know anything about how they got back on the market.

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So I'm happy -- if you want me to stick to your report, Dr. Sheinin, you have to stick to your report, too. And you brought this up six times, but you haven't looked at it at all.

MR. REEFER: Because, John, you keep asking him questions about areas that he's not going into. I mean --

BY MR. DAVIS:

Q. You've reviewed the nitrosamine testing data, have you not, Dr. Sheinin? That's in your materials considered list, is it?

MR. REEFER: Object to form. Beyond the scope.

THE WITNESS: What are you saying I reviewed?

BY MR. DAVIS:

Q. Your materials considered list, Exhibit B, refers to you having reviewed Mylan's nitrosamine testing data for its valsartan products.

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Did you actually look at that?
A. Are you referring to a spreadsheet?
Q. Yes, I am.
A. I did see the spreadsheet.
Q. Okay. And did you see that NDEA was present in every single line there in that spreadsheet, every -- in each line, representing a different lot or batch of valsartan, that there was NDEA in every single one of them? Did you see that?
MR. REEFER: Object -- object to form. Mischaracterizes the document.
Do you want to look at it, John?
MR. DAVIS: He looked at it. I'm entitled to ask him about it.
BY MR. DAVIS:
Q. Did you see the document?
You said you saw the spreadsheet that had the nitrosamine

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testing data, that's right, Dr. Sheinin, correct?
A. Correct.
Q. Okay. And did you see that every single lot or batch on that spreadsheet had NDEA in it?
A. I did not notice -- I did not look at the entire spreadsheet, so I can't say that yes or no, every single lot had NDEA -- NDEA in it. I'd be happy to look at it again.
Q. Do you think that -- do you think that NDEA would have made it into Mylan's valsartan products if they had done a sound scientific appraisal of their chemical manufacturing process?
MR. REEFER: Object to form. Beyond the scope. Calls for speculation. Foundation.
This is -- John, I'll just let you know, this will be the last question until -- you know, I asked for a break 22 minutes ago. And, you know, this is still going

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on.
So go ahead, Doctor.
THE WITNESS: That is not something that I can answer. It's organic chemistry, it's process chemistry, and I can't say yes or no. It's not within my -- the expertise that I developed over the last 50 years.
BY MR. DAVIS:
Q. It's in the FDA's warning letter to Mylan, correct?
The FDA, in their warning letter, said to Mylan that your firm had not anticipated the creation of nitrosamines in your drug product.
And that was the basis for the warning letter, was that failure, was it not?
MR. REEFER: Object to form. Beyond the scope. Foundation. Mischaracterizes the document.
THE WITNESS: FDA has said that the formation of nitrosamines

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was unexpected. They did not see it either. And they did a -- I would hope, did a very thorough review of the drug master file that was submitted by Mylan. And they did not see it.
So it's not something that I would have seen, because it's outside of my expertise. FDA did not see it either, so --
BY MR. DAVIS:
Q. Okay. Well, you're assuming --
A. -- it's not something --
Q. -- that Mylan disclosed all the facts.
You're assuming there that Mylan, in the DMF, actually disclosed the salient information to the FDA, are you not?
MR. REEFER: Object to form. Beyond the scope. Argumentative. Foundation.
He's not reviewed the DMF.

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He's not offering an opinion on the content of the DMF, whether Mylan's risk evaluation was --
MR. DAVIS: Hang on, Jason.
MR. REEFER: -- or otherwise.
MR. DAVIS: Stop with the speaking objections. He's brought up that the FDA didn't see it either. I'm entitled to ask about that.
BY MR. DAVIS:
Q. And my question about that, Dr. Sheinin, is, you're making an assumption there that the FDA had the same information in their hands that Mylan did, right, based on what was in the DMF?
MR. REEFER: Objection. Foundation. Form. Can't speak to what FDA knew or didn't know.
Go ahead, Doctor, if you can.
THE WITNESS: I mean, I have

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not seen the DMF, so I don't know what was in it.
I -- maybe I'm naive, but I did not -- when I was at FDA, I did not make an assumption that companies that submitted drug master files were not telling me the truth. So I'm at a loss there.
It's -- I don't know what was in the DMF, so I don't know exactly what FDA reviewed. But FDA has said in several of their statements on nitrosamines that the presence of nitrosamines was unexpected. So it goes beyond Mylan, it goes to all the companies who were making similar types of APIs. The FDA has said this was totally unexpected. And I believe the EMA has said the same thing, that it was unexpected.
MR. REEFER: With that said,

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John --
MR. DAVIS: Last question -- last question before lunch.
BY MR. DAVIS:
Q. You said that, you know, you had a right, when you were at FDA, to assume what was being provided to you was the truth, correct?
A. I didn't say it was a right. I said that was me, as Eric Sheinin, assuming that what was in the DMF was the truth.
Q. That's a fair --
MR. REEFER: So, John --
BY MR. DAVIS:
Q. That's a fair --
MR. REEFER: John, hold on.
BY MR. DAVIS:
Q. -- and reasonable assumption to make, right?
MR. REEFER: Hold on.
John, you said last question and, you know. That was your last question.

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MR. DAVIS: Let me -- let me tie a bow on it.
BY MR. DAVIS:
Q. That was a fair and reasonable assumption for someone in your shoes at the FDA to make, that the DMF that was being provided to them was the truth, was transparent, correct?
MR. REEFER: Object to form. Beyond the scope.
Go ahead, Dr. Sheinin, if you want.
THE WITNESS: Yes. That was my assumption. And I would think that when FDA investigators come in to the facility and are doing an inspection to make sure that the manufacturer is performing the synthetic scheme to what's in the drug master file that they would be viewing whether or not the processes that are being used to manufacture and synthesize the active ingredient are what's

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included in the drug master file.
If there was any discrepancies, I would expect an FDA investigator to note them.
MR. REEFER: So with that being said, John, how long do you need for lunch? And sort of let's talk planning a little bit.
MR. DAVIS: We can go off the record.
VIDEO TECHNICIAN: Going off the record. The time is 1:17 p.m.
- - -
(Whereupon, a luncheon recess was taken.)
- - -
VIDEO TECHNICIAN: We are back on the record. The time is 2:19 p.m.
BY MR. DAVIS:
Q. Okay. Dr. Sheinin, I'm going to mark Tab 5.
- - -
(Whereupon, Exhibit

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Sheinin-10, MYLAN-MDL2875-00894833, Valsartan Drug Master File, Section 3.2.S.3, was marked for identification.)
- - -
BY MR. DAVIS:
Q. Let me know when you have that document in front of you.
MR. REEFER: And I think, John, this is 10, Exhibit-10, that is.
MR. DAVIS: Exhibit-10, that's right.
THE WITNESS: I have it.
BY MR. DAVIS:
Q. Okay. Let me ask a prefatory question.
You told me you did not review any aspect of Mylan's DMF; is that right?
A. That is correct.
Q. Can I ask why, given that you have an entire section of your report dedicated to discussing drug master

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files?
A. I don't think that the -- whatever information that was in there was really pertinent to my discussion of drug master files in my report. I wasn't going to be opining on the adequacy of Mylan's DMF.
So in the interest of the time that I had to devote to this project, if I had gotten involved in really looking at the DMF, I probably would have just wanted to keep going and going.
So it just -- it wasn't necessary for what I was asked to look at.
Q. Well, let me direct your attention, then, before we turn to Exhibit-10, back to your report for a second.
I just want to get clarification on what you mean in Paragraph 68 of your report where you write, Mylan's valsartan USP API

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continued to meet its specification, as well as it's DMF specification, throughout this period.
What are you -- what do you mean by "DMF specification" there?
A. By DMF specification I mean what was on file with the FDA.
Q. Okay. But you didn't review the DMF?
A. That's correct. But I did look at certificates of analysis, so I could see that Mylan was in compliance with all of the acceptance criteria in the DMF.
Q. So what is -- is a DMF specification similar to a USP specification, it just has a test procedure laid forth, basically?
A. A DMF specification is, basically, the same specification that's in the ANDA. Because that's where the specification comes from, since Mylan is using a drug master file to report that information to FDA.

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So that means that the DMF specification has more in it than what's in the USP monograph.
Q. Okay.
A. Because the application specification is the same as the DMF specification, and that has additional tests in it.
Q. Is the DMF specification sort of the final output of the ANDA DMF?
A. I don't understand that question. I'm not clear.
Q. Sure.
There might be -- for example, let's take a category of testing, like residual solvent testing, that's in the DMF specification.
There's a lot of workup in the DMF regarding what to test for that's ultimately put in the DMF specification, is it not -- is there not?
A. That's correct.
Q. So the DMF specification, ultimately, is an output of all of the

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work that's done in the DMF itself, right?
A. Yes and no. I mean, there's other information in the DMF that has nothing to do with the specification.
Q. Sure. But what's in the specification is an output of what's -- of the work that's done in the DMF, is it not?
A. I've never heard it expressed in that way. It's the -- the specification is what FDA says you have to meet, your specification.
And, in general, what's in the USP monograph is in agreement with the part of the specification that those tests are included in.
Q. You wouldn't just write a DMF specification, would you? There's quite a bit of work that goes into generating a DMF specification, right?
A. Well, yeah. Yeah. Of course.
Q. And where is that work

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documented?
A. Well, part of the work that's in the specification is the analytical methods. And that's -- that's done in Section 4.2 of the application. And Section 4.3 is the validation of the analytical method.
So that -- that's -- that has to be done before you can have a specification.
Q. And where -- where is that work documented? It's documented in the DMF, is it not?
A. The method validation work is -- should be documented in the drug master file. So those -- the method validation for each one of the analytical procedures that's used to control the quality of the product should be included in the drug master file.
Q. Okay. Back to Exhibit-10, which I just marked.
Do you recognize that as the impurities section of the valsartan drug

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master file?
A. No, I've never seen this, because I didn't look at the drug master file.
Q. Right. I understand that you haven't seen this in particular.
But you've seen drug master files generally, correct?
A. Yes.
Q. And a drug master file will have an impurities section, will it not?
A. It should have an impurities section, yeah.
Q. Okay. And does what I've marked here as Exhibit-10 look like that might be the impurities section of Mylan's valsartan USP drug master file?
A. It looks like it.
Q. Okay. And you'll see on the -- there's some numbering in the bottom right corner, starting on the second page.
A. Page numbers?
Q. That's correct.

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Do you see that?
A. Yes.
Q. At the first numbered page, you'll see a table of contents for this DMF impurities section.
Do you see that?
A. Yes.
Q. And then at the very end, at Pages 80 to 82, there's a section on genotoxic impurities.
Do you see that?
A. Yes.
Q. Why are genotoxic impurities broken out as a separate category of impurities, do you know?
MR. REEFER: Object to form. Scope.
THE WITNESS: I don't know.
BY MR. DAVIS:
Q. Okay.
A. I've not seen them -- anything that I have looked at, at FDA or USP, where genotoxic impurities were broken out as a separate category of

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impurities.
I know impurities, I know inorganic impurities, residual solvents are basically organic impurities, but they are oftentimes categorized different because there's a separate analytical method. And I have never seen a list like this that had genotoxic impurities as a category.
Q. You don't think that would be because there's separate applicable guidances that govern genotoxic impurities, such as, for example, ICH M7 that I've shown you today?
MR. REEFER: Objection. Form and scope.
THE WITNESS: It's possible, but I can't say yes or no. I don't -- I don't know.
BY MR. DAVIS:
Q. Flip, if you would, to the very last two pages of this document, which are numbered 81 and 82.
A. Okay.

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Q. Do you see the header at the top of Page 81, Genotoxic Impurities?
A. Yes.

[redacted]

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[redacted]

MR. DAVIS: I'm going to mark Tab 24.

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MR. REEFER: Can we put this away?
MR. DAVIS: Yes. Tab 24, Jason.
MR. REEFER: Is that one that you sent today or --
MR. DAVIS: Yes, that's one sent today.
MR. REEFER: What's the one -- which one did you send me at lunch? Is that the one or is that --
MR. DAVIS: That's 25.
MR. REEFER: Okay. Just one moment, then, okay, John?
- - -
(Whereupon, Exhibit Sheinin-11, MYLAN-MDL2875-00392350, 11/26/18 E-mail, Owens to Smith, was marked for identification.)
- - -
MR. REEFER: They're not stapled, but I think that we

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should be able to make due. So I'm going to hand it to him now, okay, John.
MR. DAVIS: Sure.
BY MR. DAVIS:
Q. You'll see, Dr. Sheinin, that this is an internal -- or partly internal Mylan e-mail chain that has a Plaintiff Owens-2 sticker on it.
MR. REEFER: I'm going to object initially to foundation.
Is this Exhibit-11 marked, John?
MR. DAVIS: Yes, it is.
MR. REEFER: Thanks. But I object to foundation.
But go ahead, Dr. Sheinin.
BY MR. DAVIS:
Q. Sure. And I'm just making a representation to you here, Dr. Sheinin, I understand that you haven't seen this document before.
I'm representing this to you to be a partly internal Mylan e-mail

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chain with a Mylan Bates stamp, as it was produced to us, dated November 2018.
Do you see that?
A. Yes.
Q. And I say "partly internal," because if you go down to the second and third e-mails, there are some FDA e-mail addresses on the e-mails, including for Ms. Dellarese Herbert.
Do you see that?
A. Yes.
Q. Okay. And you'll see on the second page of the e-mail chain, there's an e-mail from Dellarese Herbert at FDA to several Mylan individuals that's dated November 19, 2018.
Do you see that?
MR. REEFER: Let me, just for a moment, Eric, object. I'll object on foundation.
But based on your prior representation about who is on the e-mail recipients, I'll let him answer, okay, John?

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Do you understand what I'm saying?
MR. DAVIS: Sure. Yeah.
MR. REEFER: Yeah. My point being I don't think that Dr. Sheinin knows exactly who these people are. But your representation being that those are Mylan employees, with that said, I'll let him go, okay?
MR. DAVIS: Sure. And I'm happy to ask about e-mail addresses.
BY MR. DAVIS:
Q. Do you see some FDA e-mail addresses and some Mylan.com e-mail addresses on that particular e-mail at the top of Page 2?
A. Yes.
Q. And the from e-mail address, it's dellarese.herbert@fda.hhs.gov.
Do you see that?
A. Yes.
Q. And there's several Mylan

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individuals listed in the to and cc section.
Do you see that?
MR. REEFER: Same objection.
THE WITNESS: Yes.
BY MR. DAVIS:
Q. Including a Ms. Cassandra Bird.
Is that a name you recognize?
A. No.
Q. So you wouldn't know that she was deposed in this case and that -- and that there would have been a transcript of her deposition prepared?
A. I don't know that she was deposed. I don't know who she is. I have not seen a deposition from her. I just don't know anything about her.
Q. Right. And that's because it wasn't provided to you by counsel in the package, right?
MR. REEFER: Object to form.
THE WITNESS: Correct.

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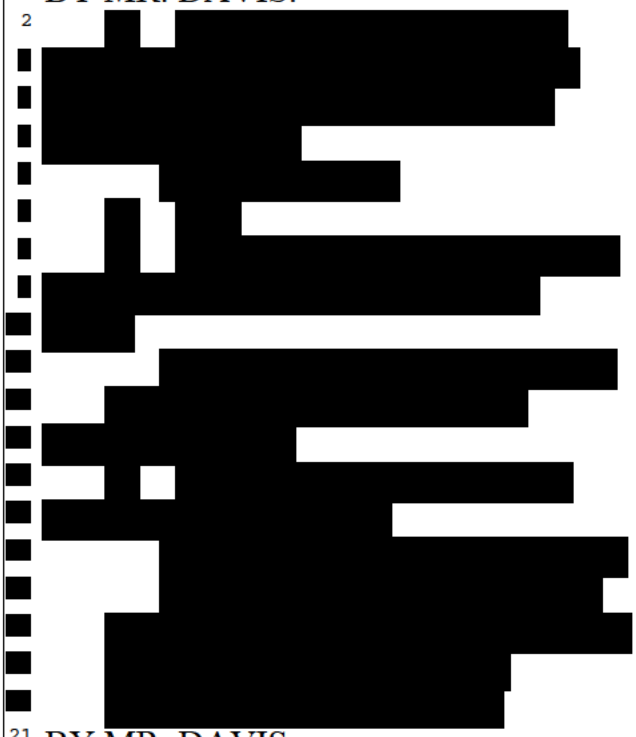
BY MR. DAVIS:



BY MR. DAVIS:
Q. Okay.
MR. DAVIS: I'm going to mark Tab 23 as Exhibit-12.

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- - -
(Whereupon, Exhibit Sheinin-12, MYLAN-MDL2875-00552465, DMF DLAPI Information Request, was marked for identification.)
- - -
MR. REEFER: Should we put 11 away, John, or keep it handy?
MR. DAVIS: We can put it away.
MR. REEFER: Okay. So now you want 23. What's on the front page, John? I'm trying to leaf through this.
MR. DAVIS: Plaintiff Talton-7 is the exhibit stamp.
MR. REEFER: Okay. Thanks.
THE WITNESS: This is going to be 12; is that right?
MR. DAVIS: Exhibit-12, that's correct.
BY MR. DAVIS:
Q. And I only am going to show

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you this for a limited reason, Dr. Sheinin. So don't fret, I'm not going to make you look at all 100 pages of it.
So you'll see --
A. Thank you.
Q. -- in the first -- the first actual page -- a lot of these documents come with a slip page at the front, which is just what's called metadata regarding the document that is as it was produced by Mylan.
But you'll see the first actual page, there's a letter from the FDA to Mylan, attention Michael Plastina.
Do you see that?
A. Yes.
Q. And it says, This communication is in reference to your drug master file for valsartan.
Do you see that?
A. Yes.
Q. Okay. If you flip to the next page, Page 2, you'll see the actual

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information requests that start at the very bottom, Numbered 1, and then 1 has A through J subparts that continue on the next pages.

Do you see that?

A. Yeah.

I was looking for the date of this letter.

Q. I can help you with that.

A. It's usually at the end.

MR. REEFER: It's November 13th, 2018. Is that what you were going to say, John?

MR. DAVIS: Yes.

BY MR. DAVIS:

Q. That's on Page 7.

MR. REEFER: Dr. Sheinin, if you need to take a moment to familiarize yourself with the document, you're entitled to do so.

BY MR. DAVIS:

Q. Do you see the date stamp, Dr. Sheinin, that appears after David

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Skanchy's signature?

A. Yes.

Q. And that date is November 13th, 2018?

A. Yes.

Q. What's your understanding of -- what's your understanding of where --

A. I was going to say --

Q. -- where that date falls in the chronology of Mylan's valsartan recall?

A. I'm not sure if it was before or after the recall. But I think it was -- this was after the recall, I believe. But I'm -- I can't say for sure.

Q. I'll represent to you that Mylan's recall of all of its lots and batches of valsartan on the market with an expiry occurred in late November and early December, after this letter --

A. Okay.

Q. -- if that gives you some

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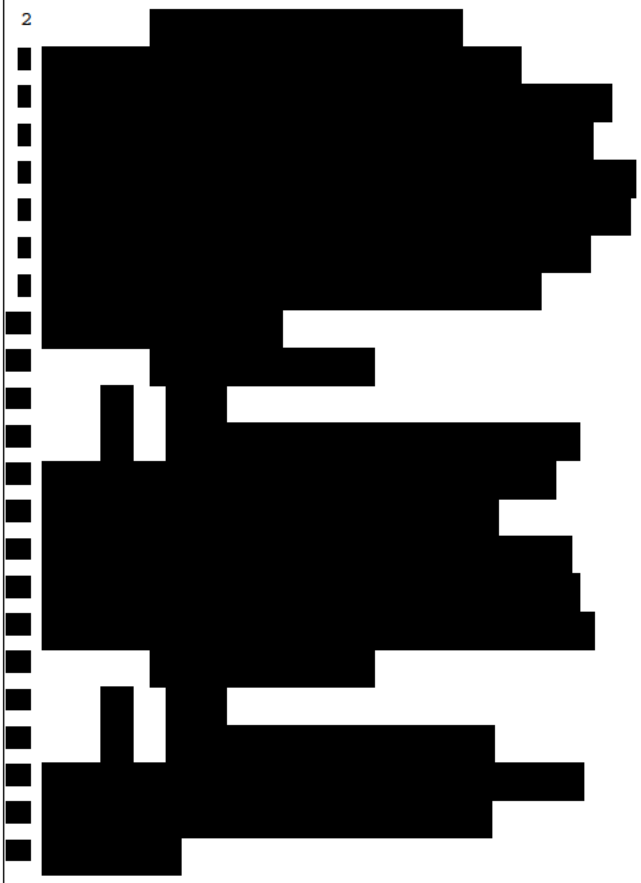
context.



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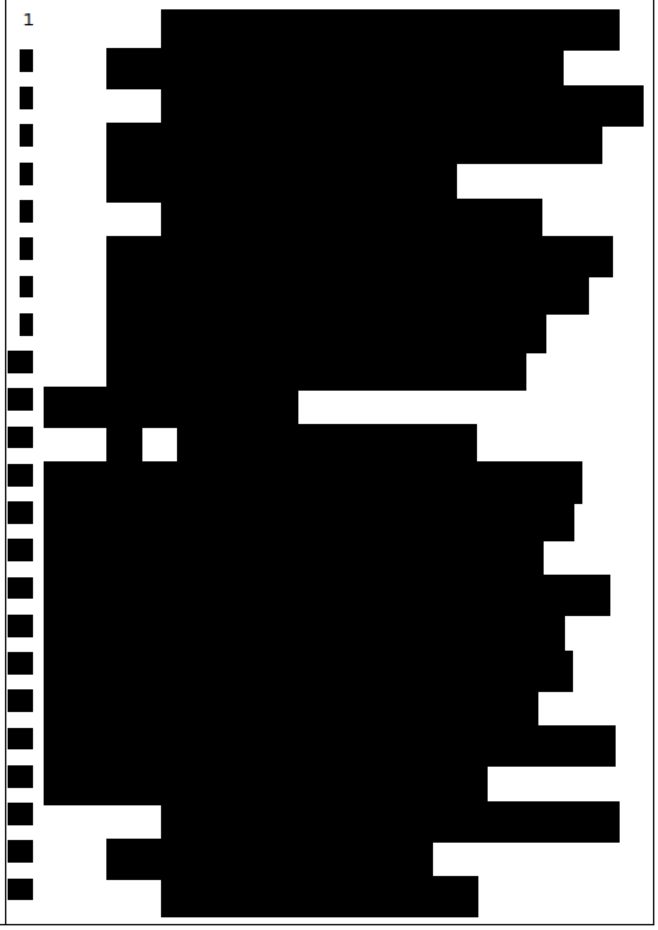

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[redacted]

Page 196

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[redacted]

Page 195

1

[redacted]

Page 197

1

[redacted]

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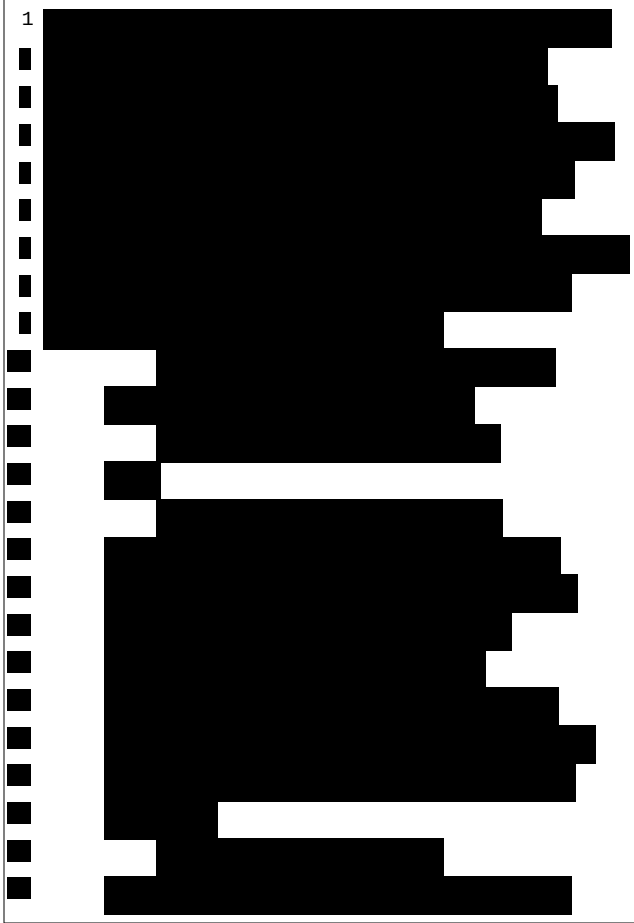

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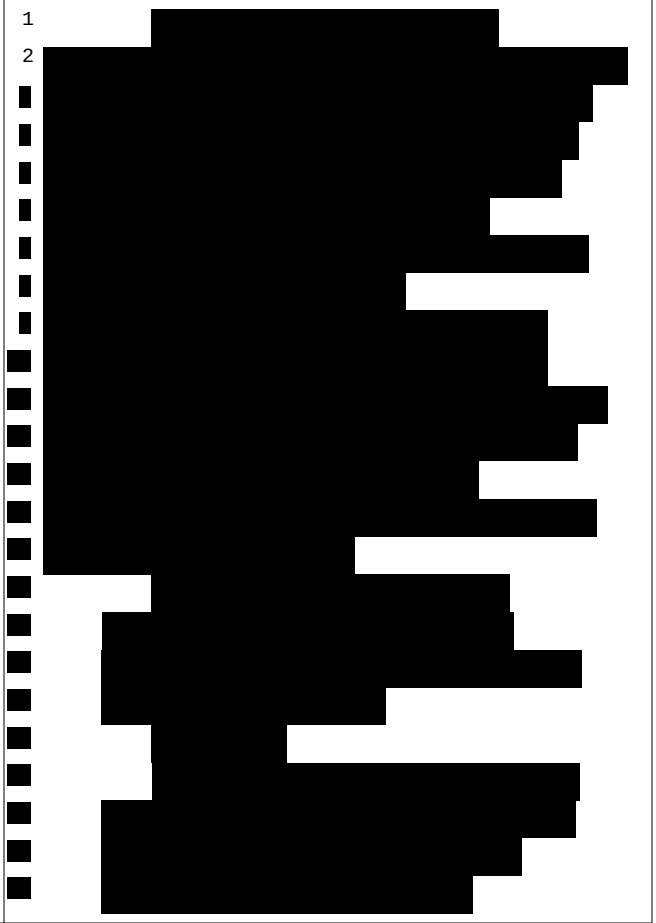

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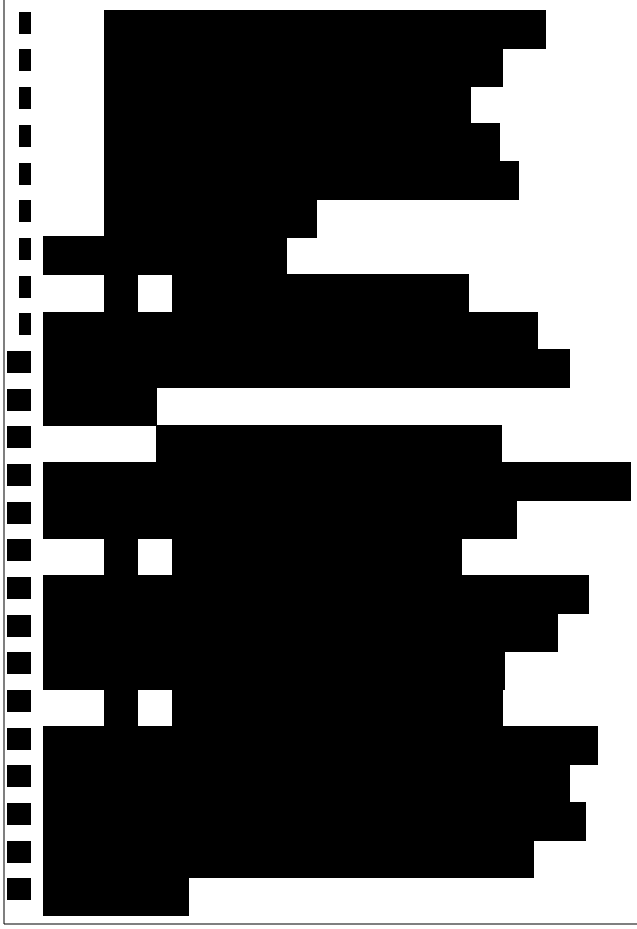

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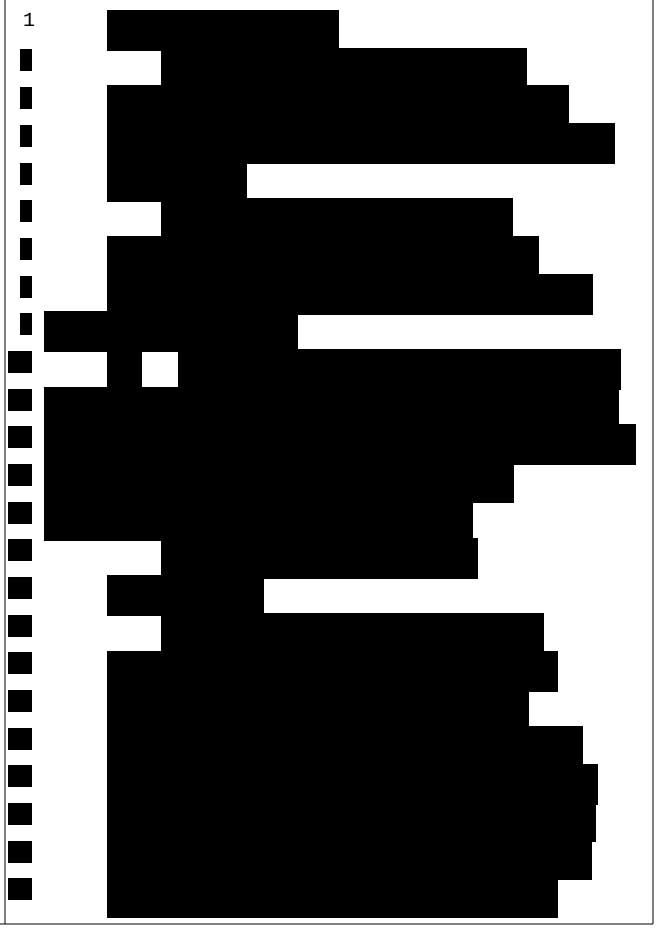

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[redacted]

MR. DAVIS: Let's mark Tab 25 as Exhibit-13.

- - -

(Whereupon, Exhibit Sheinin-13, No Bates, Valsartan Development Report, Addendum IV, was marked for identification.)

- - -

MR. REEFER: Should we put 12 aside, John?

MR. DAVIS: Yes, you may.

MR. REEFER: Okay. And 25 is the new one, right --

MR. DAVIS: That's correct.

MR. REEFER: -- that you sent during lunch?

Okay. Thank you.

BY MR. DAVIS:

Q. Did you review any development reports related to Mylan's development of its manufacturing process for valsartan API, Dr. Sheinin?

A. Not that I'm aware of. I don't believe I reviewed any development reports.

Q. You'll see some numbering, C01, C02, C03, it's kind of like stamped numbering in the bottom center of the pages.

A. Yeah. Some of them are rather blurry. But I can see there's numbers or something down there.

[redacted]

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[redacted]

Q. Did you -- in preparing your expert report, Dr. Sheinin, did you come to any kind of understanding of how NDEA was formed exactly in Mylan's valsartan API?

MR. REEFER: Object to form. Scope and foundation.

But go ahead, Doctor, if you know.

THE WITNESS: I did not come to any conclusion on that. I wasn't asked to look into it.

BY MR. DAVIS:

Q. Even though you weren't asked to look into it, do you have at least some kind of understanding of how it formed?

MR. REEFER: Same objection. Asked and answered.

THE WITNESS: I have some understanding, but I don't know the -- all the conditions and what it takes to form NDEA.

BY MR. DAVIS:

Q. Dr. Daniel Snyder's deposition testimony and exhibits are listed in your Exhibit B, materials considered, are they not?

A. I see a Dan Snyder, yes. I did not look at his report.

Q. Well, he's a -- he was a

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Mylan fact witness deposition that was taken in this case. So he wouldn't have prepared an expert report. However, his testimony largely centered on Mylan's root cause evaluation.

Do you recall reading his testimony?

A. I did not read it.

Q. Did you look at any of the exhibits to his deposition?

A. I don't know anything about him. I didn't look at it.

I think I mentioned earlier all those individuals listed at the end of my list, I did not look at any of their information, reports or depositions or anything.

Q. So it was provided to you but you didn't look at it?

A. Correct.

Q. Okay. What I've marked as Exhibit-13 here, which is Addendum IV to the valsartan development report, that's also listed in your Exhibit B, materials

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considered, is it not?

MR. REEFER: I'm sorry, John, the correct -- I think you said, maybe, the wrong exhibit number. Or did I write it down wrong?

Oh, I'm sorry. I'm so sorry, John, I interrupted you. I messed up. I wrote down Exhibit-25 because it was Tab 25. I'm sorry to interrupt your examination, John.

MR. DAVIS: Not a problem.

BY MR. DAVIS:

Q. So the question, Dr. Sheinin, is what I've marked as Exhibit-13, which is the 70-page document entitled, Addendum IV to Valsartan Development Report, that's also listed in your materials considered, is it not, under Item 8?

A. Yes.

Q. Did you review this?

A. No.

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[redacted]

Page 209

[redacted]

BY MR. DAVIS:

Q. Let me ask you, Dr. Sheinin, from a -- from a process chemistry perspective, would you assume a different result, in terms of chemical reactions, if the same process was followed every single time?

MR. REEFER: Object to

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foundation and scope.
THE WITNESS: And I'm not a process chemist, but my experience has been that when you're manufacturing batch after batch after batch of a drug substance, you're not going to end up with exactly the same impurity profile and you're not going to end up with exactly the same assay value.
So I wouldn't want to say that everything is going to be exactly the same if you run the procedure the same way, with the qualification that I'm not a process chemist.
BY MR. DAVIS:
Q. But assuming -- let's assume that, you know, all of the -- all of the variables, meaning, like, the reagents, catalysts, the temperatures, the equipment used, all of those things are the same, chemical reactions don't choose to happen sometimes and not others,

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right?
Isn't that a basic principle of organic chemistry, is that you can reliably cause chemical reactions to occur under certain conditions?
MR. REEFER: Object to the scope. Foundation. Asked and answered.
THE WITNESS: Again, when companies -- again, not being a process chemist, but companies are running their synthetic schemes, I would assume, the same way, and yet they can -- sometimes an impurity shows up, sometimes it's not.
So it's not always going to be exactly the same even though they run the procedure the same way, use the same chemicals, the same reagents, the same temperatures, the same time.
There is variation in what the results are.

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BY MR. DAVIS:
Q. Right. I'm asking more of a theoretical question, which is, isn't it a -- just a general principle of chemistry that if you -- that chemical reactions will occur in the way you would expect them to reliably?
You don't mix two things and have a completely different result one time or another; chemical reactions occur reliably as a matter of the basic discipline of the science, correct?
MR. REEFER: Object to form. Scope. Asked and answered again.
THE WITNESS: In general, chemical reactions will go the same way. But there's different -- to a different extent, I have to go back to I'm not a process chemist, but when they run the procedure the same way, they are going to find differences. So it's not going to be exactly the same every time.

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BY MR. DAVIS:
Q. You did say that you had reviewed the nitrosamine testing spreadsheet, correct?
A. Yes.
Q. And that did show NDEA present in every single lot batch that was tested, correct?
A. I believe what I said was that I did not look at the entire spreadsheet, so I can't say that it was present in every single batch.
But the page that I looked at, I did see it in those lots. But I did not look at the entire spreadsheet.
MR. DAVIS: Hey, Jason, let's take a quick break, five minutes. I'm actually almost done, I just want to review my notes.
MR. REEFER: No problem.
VIDEO TECHNICIAN: Going off the record. The time is 3:13 p.m.
- - -

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(Whereupon, a brief recess was taken.)

- - -

VIDEO TECHNICIAN: We are back on the record. The time is 3:26 p.m.

BY MR. DAVIS:

Q. The last real item I want to touch on, Dr. Sheinin, is your response to Dr. Najafi's report.

That discussion appears at Paragraphs 83 through, I guess, the end of your report; is that right?

A. Basically, yeah, I think. I don't think there's any other subheadings.

Q. Can you describe to me what -- what is your critique of Dr. Najafi's report?

A. The main critique is that he's saying that the impurity profile has to be the same for the generic to be able to say that the API is the same as is used in the reference-listed drug.

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And I believe I go on to discuss why that's not the case. And, again, I would come back to the fact that when a company makes the drug substance by one route and a second company is making it by a different route, you're going to get, almost for certain, a different impurity profile, and, still, under the definition in the regulations, those two APIs are the same.

The impurity profile is immaterial to whether or not the API is the same as what's in the reference-listed drug. And he doesn't seem to agree with that.

Q. Well, he also doesn't say that, though, does he? He doesn't say anywhere in his declaration that the impurity profiles generally have to be the same, does he?

A. From what I remember, he's saying that the impurity profiles have to be the same or it's not considered to be the same API.

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Q. But you can't point me to a particular portion of his report you're referring to where you claim that he says that?

A. I don't have it in front of me, and I'd have to read through his report again.

But that's -- that's my understanding and impression, was that he was saying that they're not the same because they have different impurity profiles.

Q. You don't cite the portion of his report you're claiming where he says that in your -- in your report, do you?

A. I don't -- I don't think so.

Q. Okay. So the answer is no?

A. 98, Dr. Najafi concludes that valsartan-containing products that contained NDMA and NDEA were not the generic equivalent of Diovan or Exforge because they contained NDMA and NDEA.

And what I'm saying is the

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drug substance used in Mylan's valsartan, by the definition in the regulations, is the same as the valsartan that's used in the innovator product. But he's saying they're not, and I'm saying that they are.

Q. Well, what's your basis for saying that they are, despite the fact that they had NDMA and NDEA and were all, by the way, recalled?

A. The basis for what I'm saying is that, as I stated a little bit ago, you can have different impurity profiles in the active ingredient and it's still considered the same as that that's used in the reference-listed drug.

That's what the regulations describe, that the API is the same. The impurity profile is immaterial to that, unless -- unless you have a case where there's an impurity that makes up 50 percent of the API.

I mean, you're not going to have that, so --

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Q. So -- go ahead, Dr. Sheinin. I didn't mean to cut you off.
A. The impurity profile is not what determines whether the API is the same in the reference-listed drug and the generic drug.
Q. So let me get -- let me see if I understand what you're saying.
You're saying, from a general -- as a general proposition, it's possible that an API can have a different impurity profile and still be considered a generic equivalent; is that what you're saying?
A. I'm saying that the API can have a different impurity profile and be considered the same as the reference-listed drug.
Q. And when you say "the same" --
A. I'm saying that the API in a generic drug can have a different impurity profile and still be considered the same as the API that's used in the

Page 219

reference-listed drug.
Q. Okay. And you're saying -- by "the same" -- what do you mean by "the same" there?
A. That under the regulations that it's considered the same ingredient if it has the same structure, the same purity -- I guess purity doesn't -- is not really a factor.
But if it has the same structure, if it's the same chemical, then it's the same, regardless of what its impurity profile is.
Q. Well, purity is a factor, though.
What -- what regulations are you referring to when you say that it doesn't have to be -- that it is the same regardless of the impurity profiles? What regulation are you referring to for your understanding of that?
A. I'd have to go back into the CFR. It could be in a guidance. But it's --

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Q. Are you familiar with the FDA's Orange Book?
A. Yes.
Q. You don't mention the Orange Book anywhere in your report, do you?
A. No, I do not.
Q. And it's not listed in your materials considered, is it?
A. It is not.
Q. Okay. When is the last time you think you reviewed the -- anything regarding the FDA's Orange Book?
A. It was at some point this year that I can remember looking -- looking at the Orange Book.
Q. In your understanding, what is the FDA Orange Book?
A. The Orange Book is --
MR. REEFER: Objection to scope.
THE WITNESS: Sorry.
MR. REEFER: Go ahead.
THE WITNESS: The Orange Book is a -- basically a

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compendium of all the products that are approved by FDA, and they're listed by active ingredient.
And it shows whether or not a generic is considered bioequivalent to the reference-listed drug, and it shows which -- which product or products are considered as reference-listed drugs.
BY MR. DAVIS:
Q. Well, bioequivalence is just one aspect of therapeutic equivalence, right, which is the larger thing the Orange Book is concerned with, correct?
A. I believe so.
Q. And the Orange Book will list, like you say, various drugs and which ones are therapeutically interchangeable with each other because of a therapeutic equivalence determination, correct?
MR. REEFER: Object to form.

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Scope.
THE WITNESS: Correct.
MR. DAVIS: Let me mark Tab 17 as Exhibit-14.
- - -
(Whereupon, Exhibit Sheinin-14, No Bates, Orange Book Preface, Food and Drug Administration, Center for Drug Evaluation and Research, Approved Drug Products with Therapeutic Equivalence Evaluations, was marked for identification.)
- - -
BY MR. DAVIS:
Q. Have you read this FDA-authored Orange Book preface before, Dr. Sheinin?
A. No, I have not.
Q. Do you see that the URL at the bottom of the page is pulled from the www.fda.gov website?
A. Yes.
Q. And you'll see on the second

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page, bottom -- bottom two paragraphs, really, the FDA says that, The therapeutic equivalence evaluations in the Orange Book reflect the FDA's application of specific criteria to the multi-source prescription drug products listed in the Orange Book and approved under the FD&C Act.
Do you see that?
A. Yes.
Q. And then the next paragraph down says that, A complete discussion of the background and basis of the FDA's therapeutic equivalence evaluation policy was published in the Federal Register in 1979.
Do you see that?
A. Yes.
Q. If you go to Page 4, you'll see a section titled, Introduction.
A. Yes.
Q. It says, The Orange Book is composed of four parts.
And the first part is,

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Approved prescription drug products with therapeutic equivalence evaluations.
Do you see that?
A. Can you read that again?
Q. The first sentence of the introduction reads, The Orange Book is composed of four parts.
And then the first part it lists is, Approved prescription drug products with therapeutic equivalence evaluations.
Do you see that?
A. Yes.
Q. Okay.
A. I see that.
Q. So would you agree that therapeutic equivalence is really the regulatory touchstone of evaluating whether a generic product is -- can be considered the same as a brand product?
MR. REEFER: Object to form. Scope.
THE WITNESS: I would say that therapeutic equivalence,

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if -- if the generic is therapeutically equivalent to the reference-listed drug, that they're interchangeable.
BY MR. DAVIS:
Q. And that's the FDA's way of saying you can -- you can take it to the bank that this drug is going to be the same as the RLD, correct?
MR. REEFER: Object to form. Vague.
THE WITNESS: My -- my way of looking at it is if FDA has approved a generic drug and FDA says it's therapeutically equivalent, that I can take the generic in lieu of taking the reference-listed drug to achieve the desired outcome for whatever reason that I'm taking the drug for.
BY MR. DAVIS:
Q. And that's what's most important here, right, for physicians'

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and patients' purposes in evaluating whether a generic is the same as the brand, right?

It's not living in some hypothetical world, it's -- there's a reason for that, which is, can I substitute it for the brand, right?

MR. REEFER: Object to form. Scope. Foundation.

THE WITNESS: Yeah. The -- again, to me, the generic means that the FDA has approved it and it's therapeutically equivalent, so I have no problem with taking the generic in lieu of taking a reference-listed drug.

BY MR. DAVIS:

Q. And that's what it means to be -- sorry. Go ahead.

A. I was going to say, the issue of sameness, we were discussing sameness of the active ingredient. I don't know that that's exactly the same as the sameness of whether it's

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therapeutically equivalent or not.

It's two different -- to me, it's two different uses of "sameness."

Q. Okay. And you're not sure what Dr. Najafi was referring to in his report, whether he was referring to the defendants at issue, VCDs being therapeutic equivalents or generic equivalents or whether the API was just the same, are you?

A. He's saying valsartan-containing drug products that contain NDMA and NDEA were not the generic equivalent of Diovan or Exforge because they contained NDMA and NDEA.

So I'm saying that they are equivalent.

Q. You're saying that they're therapeutically equivalent under the Orange Book?

A. Yes.

Q. But you haven't looked at the Orange Book at all in your report, have you?

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A. No, I have not.

Q. Okay. And you're just now looking at the Orange Book preface since I've showed it to you, correct?

A. Correct.

Q. So is this, like, an off-the-cuff opinion that you're making?

MR. REEFER: Object to form. Argumentative.

MR. DAVIS: Well, no, it's a fair question.

BY MR. DAVIS:

Q. Dr. Sheinin, you don't -- you don't put anywhere in your report the opinion that the NDMA- and NDEA-contaminated valsartan is a therapeutic equivalent to the RLD, do you? That's nowhere in your report, is it?

A. No.

Q. Okay. And do you know what criteria, even, the FDA requires for a drug to be considered therapeutically equivalent to an RLD?

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MR. REEFER: Object to form. Foundation.

Go ahead.

THE WITNESS: I know it has to be considered to be bioequivalent. I'm not sure what the second criteria is. I know that there's two factors that go into the therapeutic equivalence.

BY MR. DAVIS:

Q. So how could you form an opinion that the defendants' valsartan in this case was therapeutically equivalent to the RLD when you're not sure what the definition of therapeutic equivalence is?

MR. REEFER: Object to form. Misstates testimony. Beyond the scope.

THE WITNESS: What exactly did I say?

Najafi said that if it contains NDMA and NDEA, that it's not the generic equivalent. I did not use the words "therapeutically

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equivalent."
And, to me, the fact that NDMA and NDEA may be present does not make it not generically equivalent to the reference-listed drug.
It's the active ingredient that's important. The impurities in general do not contribute to the efficacy of the active ingredient and the drug product. So the presence of impurities is immaterial to whether or not the generic is equivalent to the reference-listed drug.
BY MR. DAVIS:
Q. Well, the FDA is not just concerned with efficacy, they're also concerned with safety, aren't they?
MR. REEFER: Object to form. Beyond the scope.
THE WITNESS: They are. And FDA has said that there is a very -- what's the word I'm

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looking for -- theoretical issue with nitrosamines and that there's a very minimal risk and that these impurities are present at extremely low levels, they are trace impurities. And there are products that FDA has allowed on the market that do contain nitrosamines.
BY MR. DAVIS:
Q. I thought you told me you're not a toxicologist, right, so you have no way to independently evaluate any of those assertions, right?
A. That's correct. I'm not a toxicologist, but I can read what's written in the FDA statements, that it's a theoretical risk.
And it may -- I think it says further in those statements that it may be a cause of cancer; it may.
As a scientist, I don't have to be a toxicologist to understand what FDA is saying there.

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Q. The FDA did require the recall of every single lot and batch of Mylan's valsartan, did they not, though?
MR. REEFER: Objection to form. Misstates facts. Beyond the scope.
THE WITNESS: I believe that, yes, FDA recalled all the lots of Mylan's valsartan products.
BY MR. DAVIS:
Q. And you're aware that the IARC, EPA and other regulatory bodies that evaluate toxicology have classified NDMA and NDEA as probable human carcinogens, correct?
MR. REEFER: Object to form. Foundation. Beyond the scope.
MR. DAVIS: He's -- Jason, he's the one who just brought this up. I've got to delve into it now.
MR. REEFER: He -- John, he clarified that he was --

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MR. DAVIS: No, he didn't, Jason. He went off on a tangent, and now I've got to -- now I have to put the lid back on it.
BY MR. DAVIS:
Q. So you can answer the question, Dr. Sheinin.
Are you aware that the IARC, EPA and other regulatory bodies governing toxicology assessments have classified NDMA and NDEA as probable human carcinogens? Are you aware of that?
MR. REEFER: Object to form. Foundation. Beyond the scope.
THE WITNESS: I know that I -- IA-what -- IAR-whatever was mentioned in the M7, I believe, in that paragraph you had me look at.
But other than that, I don't know anything else about that organization or what EPA has said or what any other organization has said.
BY MR. DAVIS:

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Q. Are you aware that these entities are so certain that NDMA and NDEA are human carcinogens that it's considered unethical to actually do the studies to confirm that?

MR. REEFER: Object to form. Sorry.

Object to form. Beyond the scope. Foundation.

THE WITNESS: No, I'm not aware.

BY MR. DAVIS:

Q. Okay. Are you aware that Mylan's valsartan at times contained up to 20 times what the FDA considers safe, acceptable intakes for NDEA?

MR. REEFER: Object to form. Misstates testimony and evidence.

But go ahead, Doctor.

THE WITNESS: I'm not aware of -- I didn't do any calculations to see how much above or below the -- what FDA recommended. That's all I can say.

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I did not do any kind of calculation to determine that.

BY MR. DAVIS:

Q. Okay. Thank you.

So in Paragraph 99 of your report, you say, As presented above, valsartan manufactured by a different route of synthesis that resulted in a different impurity profile still would be considered the same as that used in the RLD.

Do you see that?

A. Yes, I see that.

Q. You're not saying there that valsartan that contains NDMA and NDEA would still be considered the same as that -- as that used in the RDL, are you?

Is there a reason you're not saying that -- is there -- let me strike that and rephrase it.

Is there a reason that Paragraph 99 reads the way it does as opposed to stating the following, which would be, valsartan that contains NDMA and NDEA would still be considered the same as the RLD?

MR. REEFER: Object -- object to form. Vague.

But go ahead, Doctor, if you understand.

THE WITNESS: That's the way I always refer to the active ingredient in a generic drug versus the active ingredient in the reference-listed drug.

To me, it's always the same. If you have different routes of synthesis, and even if you have a different impurity profile, it's still going to be the same active ingredient.

BY MR. DAVIS:

Q. Well, the FDA, in that situation, would have approved that different route of synthesis, correct?

A. Correct.

Q. Okay. Have you seen any evidence that the FDA approved valsartan products where there was an affirmative disclosure that they contained NDMA and NDEA?

MR. REEFER: Object to form. Scope.

THE WITNESS: I have no way to access whether or not there was a valsartan that claimed to have NDMA or NDEA in it and that application was submitted to the FDA and that it was approved. I have no way of knowing that. So I can't say if that's a possibility.

That information is confidential and the FDA would not release that. I don't have access to FDA's information anymore.

BY MR. DAVIS:

Q. Is it your position that purity has nothing to do with therapeutic equivalence?

MR. REEFER: Object to form. Misstates the testimony. Beyond the scope.

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THE WITNESS: As long as the drug substance meets the purity acceptance criteria in the assay in its specification, the purity is going to vary for a number of reasons.

And I don't believe that that -- that a purity on one API that was in the acceptance criteria for the assay would be considered not to be equivalent to the reference-listed drug active ingredient that had a different assay value.

So there's -- that's why, in many cases, the active ingredient has an acceptance criteria of 98.0 to 102.0 percent.

BY MR. DAVIS:

Q. What about quality, is it -- do you have any understanding of whether quality has anything to do with therapeutic equivalence?

MR. REEFER: Object to form.

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Vague. Beyond the scope.

THE WITNESS: As long as the generic or any -- any drug substance meets the acceptance criteria in the specification, then -- and that includes not only the assay but the impurity testing, then I would consider that to be the same as any other API of that same chemical that has also met the acceptance criteria in the specification.

BY MR. DAVIS:

Q. Okay. Let me ask a hypothetical to you, Dr. Sheinin.

The specification lists impurities of not more than .1 percent in this case, right, for valsartan? That's what the specification says, right?

A. The specification for any other unknown impurity is point -- not more than .1 percent.

Q. Right. Let's say there was some other unknown impurity that was

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guaranteed to kill anyone who ingested the product at levels below .1 percent, percent mortality rate, are you saying that that would be considered the same, from a purity or quality standpoint, as the RLD?

MR. REEFER: Object to form. Assumes facts. Incomplete hypothetical.

Go ahead.

THE WITNESS: That's a very hypothetical question that has no place in the real world.

But in the specification, if it's -- if it's -- has -- if it meets the specification, then it's the same.

BY MR. DAVIS:

Q. Okay.

A. You have to have other -- other testing and other things to come into play for it to be considered not the same.

Q. Okay. Turn to Page 7 of

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Exhibit-14, which is the FDA Orange Book preface.

A. Okay.

Q. You'll see there's a definition provided there for therapeutic equivalence.

Do you see that?

A. Yes.

Q. And it says, FDA classifies as therapeutically equivalent those drug products that meet the following general criteria.

Do you see that?

A. Yes.

Q. Okay. One, they are approved as safe and effective.

Do you see that?

A. Yes.

Q. Do you know -- back to my earlier question.

You don't know whether the FDA has ever approved any valsartan drug product -- or, rather, any product at all that contains NDMA or NDEA as safe and

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effective, with the disclosure that it actually contained NDMA or NDEA, correct?
A. I have no way of knowing that.
Q. Do you have any understanding of whether NDMA or NDEA have any therapeutic benefit?
MR. REEFER: Object to form. Foundation and scope.
But go ahead, if you know.
THE WITNESS: I don't know whether they have any therapeutic benefit. I -- I have not looked into that.
I don't -- I don't believe they act -- act to enhance the therapeutic effect of the valsartan, but I don't know what their -- what could possibly be their therapeutic benefit.
But I can't answer that question. I don't know.
BY MR. DAVIS:
Q. Okay. The second criteria

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for meeting therapeutic equivalence is, 2, They are pharmaceutical equivalents in that they contain identical amounts of the identical active drug ingredient in the identical dosage form and route of administration.
Do you see that?
A. Yes.
Q. 2A?
A. I see that.
Q. Is that -- is that what you're talking about when you're saying that the API is the same because it meets the spec? Are you saying that valsartan API would be pharmaceutically equivalent under 2A there?
A. I would say under 2B, Meet compendial or other applicable standards of strength, quality, purity and identity.
If you take A and B together, yes, that's what I'm saying.
Q. Okay. But you're -- you conceded, though, that there are -- that

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other applicable standards out there other than USP, correct? For example, the ICH guidelines?
MR. REEFER: Object to form. Misstates testimony.
THE WITNESS: ICH guidelines do not set acceptance criteria for any particular test --
BY MR. DAVIS:
Q. For ICH M7 it does, though. We saw that in ICH M7.
ICH M7 does set thresholds. In fact, that's how the acceptable intakes for NDMA and NDEA were created by the FDA.
MR. REEFER: John, you interrupted -- John, you interrupted his answer. I'd like to --
MR. DAVIS: My apologies.
MR. REEFER: -- give him a chance to finish.
THE WITNESS: I'm talking about the ICH quality guidelines.

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I will give you that the ICH Q3C and Q3D do set standards for the amount of residual solvent and the amount of inorganic impurities or elemental impurities.
But beyond that, they do not set standards for what the assay has to be, what the level of impurities have to be. There are impurity guidelines that talk about various categories, but they don't say that the acceptance criteria for a given impurity in a given drug substance or drug product has to meet a certain level.
That's what I'm saying. And that's the guidelines and guidances that I was talking about. Where it talks here about, meet compendial or other standards, to me, that's the specification that's on file with -- in their application at

FDA.
BY MR. DAVIS:
Q. We saw that ICH M7 sets acceptance criteria, correct?
MR. REEFER: Object to form. Misstates the document.
But go ahead, Doctor.
THE WITNESS: The little bit of M7 that I know, it has information in there about these impurities. But I don't know that they actually said acceptance criteria. I'd have to go back and study that guideline.
BY MR. DAVIS:
Q. Okay. You haven't studied it for your report here?
A. Correct.
Q. Or for your conclusion in Paragraph 99 of your report, have you?
A. Correct.
Q. And you haven't even studied the FDA's Orange Book definition of therapeutic equivalence here for

Paragraph 99 of your report, have you?
A. I have not.
Q. Do you see Number 5 a little bit further down?
A. Yes.
Q. And they are manufactured in compliance with current good manufacturing practice regulations.
Do you see that as a requirement that the FDA has for a drug product to be considered therapeutically equivalent?
A. Yes.
MR. DAVIS: Just a little recordkeeping. I'm going to mark Tabs 20, 21 and 22 as Exhibits-15 through 17.
- - -
(Whereupon, Exhibit Sheinin-15, No Bates, 12/31/21 ProPharma Group Invoice #PPGUS000581, was marked for identification.)
- - -

(Whereupon, Exhibit Sheinin-16, No Bates, 1/31/22 ProPharma Group Invoice #PPGUS000820, was marked for identification.)
- - -
(Whereupon, Exhibit Sheinin-17, No Bates, 2/28/22 ProPharma Group Invoice #PPGUS001080, was marked for identification.)
- - -
MR. DAVIS: Do you have those, Jason? Those are the invoices.
MR. REEFER: Yeah, I was -- I was understanding it was just housekeeping, I wasn't about to pull them up. Do you want me to?
MR. DAVIS: Sure. I do want him to see them and verify them for me, so.
MR. REEFER: Sure. Sorry, I just -- I thought you were just

going to attach them and move on. Remind me what you're looking at, 20 --
MR. DAVIS: 20 through 22, which are now Exhibits-15 through 17.
MR. REEFER: Three one-page documents, correct?
MR. DAVIS: That's right.
MR. REEFER: I'm marking the one dated 12/31/21 as Exhibit-20 --
MR. DAVIS: Okay.
MR. REEFER: -- is that correct?
MR. DAVIS: Yes. And then do the January one for 21.
THE WITNESS: 15, 16 and 17 he said -- oh --
MR. DAVIS: Yes.
THE WITNESS: 15, 16 and 17.
MR. DAVIS: Yes. Thank you, Dr. Sheinin.
December would be

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Exhibit-15. January, 16 and February, 17.

MR. REEFER: All right.

BY MR. DAVIS:

Q. Okay. Just a few brief housekeeping questions on these, Dr. Sheinin.

Did you prepare these invoices or did somebody else prepare them?

A. Somebody else. I report my time on a timekeeping system, and I can't -- there have been -- let me back up.

I used to file a time report with NDA Partners, and then they went to a timekeeping system, and I was using that. And then they went to a different timekeeping system.

So I don't know at what point in time that this new timekeeping system went into effect. But I think it's -- since it's talking -- all these are ProPharma Group, I believe it's the

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current system.

And I enter my time on a daily basis if I'm doing any work for NDA Partners. And I then enter the, in a comment field, what work I did that day, and it goes on a weekly basis.

Q. Okay. So even if you didn't generate the actual invoice, the description notations and dates, quantities, et cetera, that's stuff you would have written in your own words, correct?

A. Correct.

Q. Okay. Are there any invoices prior to -- if you look at Exhibit-15, which is the December invoice, did you do any work on this case prior to December 13th or would that have been the first time you encountered work on this case?

A. I believe that's the first time.

Q. Okay. And then the last -- Exhibit-17, the last entry is February

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17th, 2022.

Do you see that?

A. Yes.

Q. Could you estimate for me the amount of time you've billed in this case since February 17?

A. Not counting today?

Q. Sure. Not counting today.

A. I think it's somewhere in the neighborhood of 15 to 17 hours this month. But I can't say for certainty.

Q. Okay. Would all of that time have been part of preparing for your deposition today?

A. I believe so.

Q. Can you recall doing any work after February 17 that was not dedicated to preparing for today?

A. No, I -- I mean, I -- this is when -- I reviewed the certificates of analysis and I looked at some additional FDA statements. But it was all in relation to getting ready for today.

Q. Okay. Would that be the

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supplement to Exhibit B to your report, where you say you reviewed the deposition of Ron Najafi?

A. Yes.

MR. DAVIS: Let me -- just another housekeeping matter. Let me introduce that into evidence.

- - -

(Whereupon, Exhibit Sheinin-18, No Bates, Supplement to Exhibit B to the Report of Eric Sheinin, Ph.D., was marked for identification.)

- - -

BY MR. DAVIS:

Q. Okay. I've marked that as Sheinin-18. And I don't need -- actually, here, what I'll do is just screen share it.

Can you see that on your screen, Dr. Sheinin?

A. Yes.

Q. It's a supplement to

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Exhibit B, the report of Eric Sheinin, Ph.D., Deposition of Ron Najafi.

A. I see that.

Q. Was there anything else you reviewed since submitting your expert report on January 12th that didn't make it into this supplemental exhibit, supplement to Exhibit B?

A. I don't believe so.

Q. Okay.

MR. DAVIS: Okay. That's all the questions I have for you today, Dr. Sheinin. Thank you for your time.

I'll pass the witness.

THE WITNESS: Thank you.

MR. REEFER: Does anyone have questions on the phone or remote?

Hearing none, John, let me -- let's go off the record.

VIDEO TECHNICIAN: We're going off the record. The time is 4:15 p.m.

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- - -

(Whereupon, a brief recess was taken.)

- - -

VIDEO TECHNICIAN: We're back on the record. The time is 4:51 p.m.

MR. DAVIS: For the record, before you start your questions, Jason. I'll note that we've been on a break for over 30 minutes since I concluded my questioning.

We'll reserve all rights regarding how this is all going to be allocated in terms of cost. So I'm going to reserve all that on the record.

You can go ahead, Jason.

MR. REEFER: I can also respond. John, what's the basis for your suggestion that my taking -- I don't know if it was 30 minutes or not, but what's the basis for your suggestion that I

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owe you costs for a 30-minute break in a deposition?

MR. DAVIS: If we get a bill for Dr. Sheinin's deposition time, there will be a dispute over this time period.

MR. REEFER: Okay. Well, I guess you can raise that dispute when you get the bill.

MR. DAVIS: Okay.

MR. REEFER: I don't -- I don't understand the basis of your objection. But let's just move on, okay?

MR. DAVIS: Okay. Go ahead.

MR. REEFER: Thank you.

- - -

EXAMINATION

- - -

BY MR. REEFER:

Q. Dr. Sheinin, I just have a few questions to clarify some of the testimony that you've offered thus far today. I'll be as brief as I can,

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recognizing it's already been a long day.

Do you remember, Dr. Sheinin, this morning Mr. Davis asked you a few questions about some of the prior litigation work you've done as an expert witness?

A. Yes, I remember.

Q. Okay. And one of the questions Mr. Davis asked you was whether your prior work as an expert witness was all performed on behalf of pharmaceutical manufacturers.

Do you recall that question?

A. I don't recall it in that exact way.

Q. Do you recall that during Mr. Davis's previous questions to you, he asked whether, during your prior work as an expert consultant, that work was performed on behalf of pharmaceutical manufacturers?

A. It was.

Q. And just to be clear, that prior work as an expert consultant

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involved litigation featuring pharmaceutical manufacturers as both plaintiffs and defendants, correct?
A. Yes.
Q. Were the only --
MR. DAVIS: Objection. Leading.
BY MR. REEFER:
Q. Were the only parties to those lawsuits pharmaceutical manufacturers?
A. Yes.
Q. So, therefore, if you were going to be involved as an expert consultant, would you have any choice but to represent a pharmaceutical manufacturer?
MR. DAVIS: Object to form.
THE WITNESS: I doubt that anybody would hire me.
BY MR. REEFER:
Q. And to the best of your recollection, did you represent pharmaceutical manufacturers that were

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both plaintiffs and defendants?
A. I believe so.
Q. Dr. Sheinin, I think marked as Exhibit-3 was a warning letter issued to Unit 8, dated November 5th, 2019.
Do you recall talking about that with Mr. Davis?
A. Yes.
Q. Does a warning letter constitute final agency action by the FDA?
A. No, it doesn't.
Q. Have you reviewed FDA's website to determine whether Mylan, at any point in time, has been placed on an import alert?
A. I have. I could not find any -- any time that Mylan had an import alert. I don't know how far back the database goes, but it came back and said no -- no response or something to that effect.
Q. So based on your review of information published by FDA, you've seen

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no evidence to suggest Mylan was placed on import alert following the recall of valsartan, correct?
A. Correct.
Q. Under the FDCA, can FDA permit the sale of drug product known by the agency to be adulterated or misbranded?
A. I don't believe so. I would think not.
Q. If you assume that Mylan's Unit 8 continued to manufacture drug substance for the United States market from the time of the recalls to present, would that confirm in your mind that FDA did not consider drug substance from Unit 8 to be misbranded or adulterated?
A. Yes.
MR. DAVIS: Wait. Objection to form. Objection. Leading.
BY MR. REEFER:
Q. Do you remember, Dr. Sheinin, having a discussion with Mr. Davis about the M7 guidance?

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A. Yes.
Q. Did you testify that the M7 guidance was not one which you regularly worked with during your time at FDA?
A. I don't believe I worked with it at all at FDA.
MR. REEFER: And for the record, I think the M7 guidance was marked as Exhibit-5, but I don't want to mess that up.
BY MR. REEFER:
Q. If you'd pull out Exhibit-5, please, Dr. Sheinin.
A. Okay.
Q. Dr. Sheinin, do you recall a portion of your testimony with Mr. Davis where he asked you to read beginning on Page 5 of Exhibit-5 under the heading, General Principles?
A. Yes, I remember. In fact, I had to read this -- parts of two pages, right?
Q. Correct. Yes, sir.
Dr. Sheinin, if you look at

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the second paragraph under general principles, you'll see a sentence beginning with, A threshold of toxicological concern.

Do you see that paragraph, sir?

A. Yes.

Q. And in the second sentence, does this document state that, The methods upon which the TTC -- that being the threshold of toxicological concern -- is based are generally considered to be very conservative since they involve a simple linear extrapolation from the dose, giving a 50 percent tumor incidence to a 1 in 106 incidence, using TD50 data for the most sensitive species and most sensitive site of tumor induction?

Do you see that language, sir?

MR. DAVIS: Before you answer, Dr. Sheinin, let me place an objection on the record here.

He's testified a billion

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times today he's not a toxicologist, so asking him about the substance of how thresholds for toxicological concern are created is totally outside of -- not only of his report but also of his expertise, as he's admitted today.

And I'll object to form, just for the heck of it.

MR. REEFER: I understand your position to be that the section of M7 that you required my witness to read cannot now be read into the record; is that your position, counsel?

MR. DAVIS: No, I'm objecting to where this is going, which is -- which is --

MR. REEFER: You don't know -- John -- you have no idea where this is going, John.

MR. DAVIS: I have a pretty good idea. All right, go ahead

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and answer the question.

Object to form.

BY MR. REEFER:

Q. Yes.

The question was, do you see that language; yes or no?

A. Yes.

Q. If you turn the page, Dr. Sheinin, to Page 6 of the M7 guidance marked as Exhibit-5, you'll see some language, a sentence beginning with the words, The use of a numerical cancer risk value.

Do you see that, sir?

A. Yes.

Q. And does the M7 guidance say, The use of a numerical cancer risk value (1 in 100,000) and its translation into risk-based doses (TTC) is a highly hypothetical concept that should not be regarded as a realistic indication of the actual risk.

Did I read that correctly, sir?

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MR. DAVIS: Object to form.

MR. REEFER: What's the nature of the objection, counsel?

MR. DAVIS: I said object to form.

You can go ahead.

MR. REEFER: Right. I just wanted to clarify the nature so I can fix it.

MR. DAVIS: Well, it's the inherent nature of asking this witness about concepts that he's not an expert in. You're asking him to read a sentence that he doesn't understand.

MR. REEFER: Did you ask him to do the same thing, counsel?

MR. DAVIS: No, I didn't. I asked him -- I had him clarify that he's never seen this document, didn't look at it, didn't consider it.

MR. REEFER: And did you ask him to read it, counsel?

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MR. DAVIS: Sure. Yeah, I asked him to read it to -- in order to -- in order to get the testimony that he never looked at it and never considered it.

MR. REEFER: Okay. Thank you.

BY MR. REEFER:

Q. Let me continue, Dr. Sheinin.

The next sentence reads, Nevertheless, the TTC concept provides an estimate of the safe exposures for any mutagenic compound. However, exceeding the TTC is not necessarily associated with an increased cancer risk, given the conservative assumptions employed in the derivation of the TTC value.

Do you see those sentences, Doctor?

A. Yes.

MR. DAVIS: Objection.

BY MR. REEFER:

Q. The exact sentence reads --

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MR. REEFER: I haven't finished my -- I haven't finished stating my question.

BY MR. REEFER:

Q. The next sentence reads, The most likely increase in cancer incidence is actually much less than 1 in 100,000.

Did I read that correctly?

A. Yes.

Q. The next sentence reads, In addition, in cases where a mutagenic compound is a noncarcinogen in a rodent bio assay, there would be no predicted increase in cancer risk.

Did I read that correctly?

MR. DAVIS: Jason, are you just going to ask him to confirm that you're reading sentences in the document? Or are you going to actually ask him any questions about this stuff that he doesn't understand?

MR. REEFER: I am --

MR. DAVIS: This is an utter

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waste of time. This is an absolute waste of time, if this is what you're doing.

MR. REEFER: Counsel, I am putting on the record what you asked my witness to read so as to allow you to ask him questions.

MR. DAVIS: I didn't ask him anything about derivation of TTCs or how they were derived for nitrosamines, because he doesn't know anything about that. He's not a toxicologist.

This is -- this is an absolute waste of time. You all have other experts -- had other experts who have opined on this stuff, some of whom have been struck.

But you all had plenty of experts that could -- they can talk about this. This is not one of those experts, as he himself has testified.

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This is a waste of time. I'm going to make that a continuing objection. Keep going, if you like.

MR. REEFER: Thank you.

BY MR. REEFER:

Q. The next sentence, Dr. Sheinin, I believe, reads, Based on all of the above considerations, any exposure to an impurity that is later identified as a mutagen is not necessarily associated with an increased cancer risk for patients already exposed to the impurity.

Did I read that correctly?

A. Yes, you did.

Q. Is it true that a new drug application or abbreviated new drug application may contain standards and specifications in addition to what's found in a compendial monograph?

A. Yes.

Q. Do you remember counsel asking you questions with respect to

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Exhibit-6, the valsartan drug substance monograph?
A. Yes.
Q. If you look -- if you focus simply on the monograph, irrespective of any other standards or specifications that might be in place, is it true that so long as nitrosamine impurities were not detected above 0.1 percent, the drug substance would comply with compendial standards?
A. It would.
Q. To this day, to the best of your knowledge, does FDA permit the sale of drug products within the United States containing NDMA or NDEA, so long as those levels are below acceptable intake limits?
A. I believe that's true.
MR. DAVIS: Object to form.
BY MR. REEFER:
Q. Dr. Sheinin, you were asked a series of questions related to, I think, three or four consecutive

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exhibits, including an e-mail exchange, DMF information requests, and a process validation report.
Do you remember generally that line of questioning from Mr. Davis?
A. Oh. Yeah, I remember.
[redacted],

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[redacted]

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[redacted]

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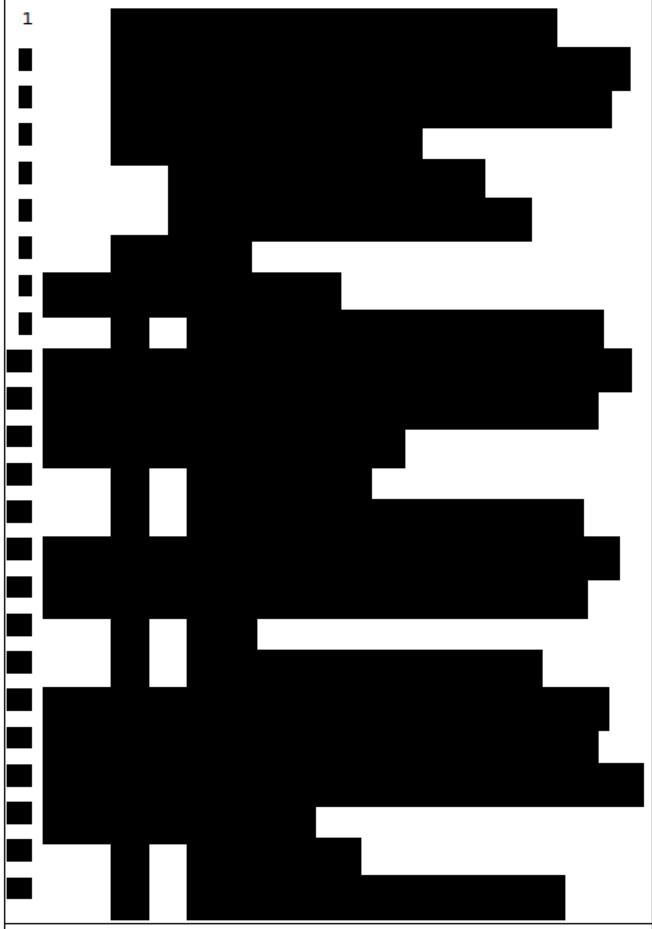

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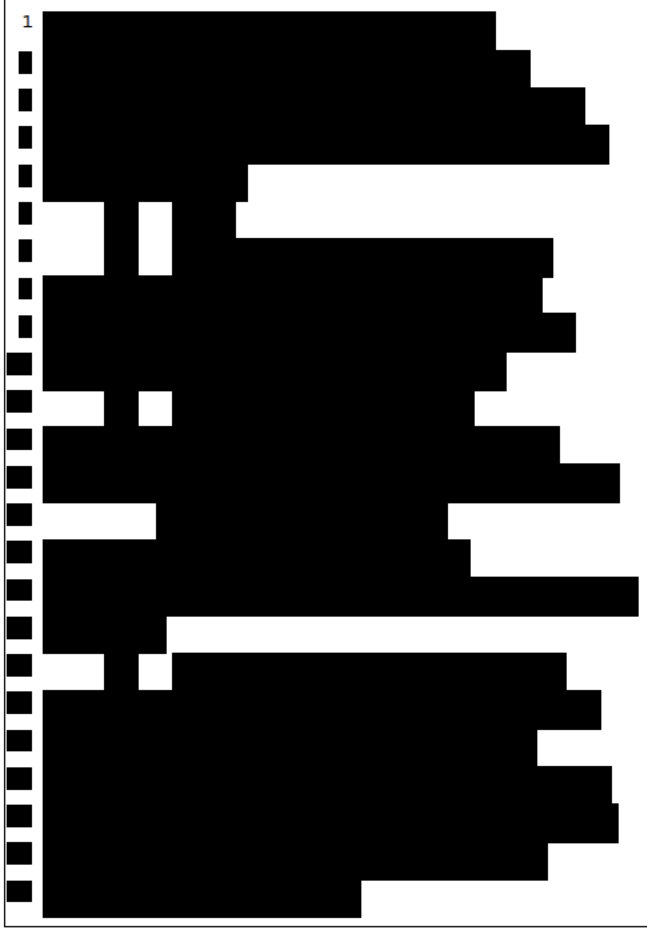

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Q. You had discussed, Dr. Sheinin, concepts about whether the impurity profile between a generic drug and an innovator or reference-listed drug must be identical.

Do you remember that discussion?

A. Yes.

Q. Do you understand that oftentimes what's referred to as a reference-listed drug is an NDA holder or what some people refer to as an innovator drug?

A. Quite often it is. It's not necessarily, but not -- most of the time, yeah. It's pretty -- pretty common.

Q. For -- and I'll refer to, you know, an NDA holder as an innovator drug; is that okay, for shorthand?

A. Yes, okay.

Q. In your experience at FDA,

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will you see batch-by-batch variants in the impurity profiles of API used to manufacture innovator drugs?

A. Yeah. I think I mentioned that during testimony today, that there's going to be variation from batch to batch and even sometimes there's -- a given impurity is not present at the time of manufacture and sometimes it is, especially if it's a very low-level impurity.

Q. Dr. Sheinin, in your experience at FDA, are you aware of instances where the manufacturer of an innovator drug sources API from multiple sources?

A. Yes. Sometimes they do that in their original NDA, sometimes they do it, through a supplement, to add another manufacturer. And I have seen NDAs where there were more than two manufacturers, especially for a, quote/unquote, blockbuster drug, where there's times that one -- one source of a drug

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substance is having issues and companies need to have alternate sources.
Q. When a manufacturer of an innovator drug sources API from multiple sources, do those API manufacturers have to use identical processes?
A. They don't have to. Sometimes the innovator may have the patent on the synthetic scheme and they want their suppliers to use the same scheme. Sometimes that's not the case and whoever they are purchasing the drug substance from is using different routes of synthesis.
Q. When an innovator drug manufacturer sources API from multiple manufacturers and those API manufacturers utilize separate and distinct manufacturing processes, would you expect there to be differences in the impurity profile of the API?
A. Definitely, I would.
Q. Does the FDCA adopt the USP compendial standard as the standard by

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which products are evaluated for adulteration?
A. Yes. I think that's in my report.
Q. If a product complies with the compendial monograph, does that mean it's not adulterated?
MR. DAVIS: Objection. Calls for a legal conclusion that he was unwilling to provide to me in his direct testimony here.
BY MR. REEFER:
Q. Do you offer the opinion that the standards set forth in Mylan's DMF were consistent with the valsartan USP monograph for a drug substance?
A. Yes. The fact that valsartan -- Mylan's valsartan is on the market and being sold in the U.S., to me, that says the quality of the valsartan API is in conformance with the USP monograph.
Q. And you did not need to review the drug master file for that

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opinion, did you?
A. No, I did not. I also looked at, I think I had mentioned earlier, two certificates of analysis. And I compared the test in the certificates of analysis with the USP monograph and found them to be in agreement.
Q. Did -- have you had an opportunity to review the label from Mylan's valsartan drug product?
A. I have. And I -- I looked at the package insert. And in Section 11, where it talks about the description, I could see that the heading there was valsartan tablets USP. And in the discussion of the active ingredient, it says valsartan USP.
Q. And does that -- why is that significant to you?
A. Because that means the -- both the drug product and the drug substance meet the requirements set forth in the compendial monographs for those

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two items.
Q. Does the potential presence of NDEA, at levels up to 1.57 parts per million, change your opinion that drug substance manufactured in accordance with the specifications set forth in Mylan's DMF would be compliant with compendial standards?
A. There's not --
MR. DAVIS: Object to form.
BY MR. REEFER:
Q. Okay. Can you explain why that is?
COURT REPORTER: I'm sorry. I need that answer repeated.
MR. REEFER: Could you repeat your answer, Dr. Sheinin.
THE WITNESS: I think I said, no, it does not.
BY MR. REEFER:
Q. And can you explain why it does not?
A. Because at 1.57 PPM, it would still meet the acceptance criteria

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in the test for any other impurity of 0.1 percent.
Q. Do you remember a portion of your report where you discuss whether routine testing performed on drug substance would have allowed for the detection of trace levels of nitrosamine impurities?
A. I do recall.
Q. Is it your opinion that routine testing would not have detected levels of NDEA as found in some batches of Mylan's drug substance?
MR. DAVIS: Objection. Object to form.
THE WITNESS: Yes.
MR. DAVIS: Objection. Vague as to what "routine testing" means.
MR. REEFER: Was your answer yes?
THE WITNESS: The answer is yes.
BY MR. REEFER:

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Q. And what's the basis of that opinion?
A. The basis of my opinion is the 30 years I had at the FDA, both in the laboratory and as a supervisory review chemist, and my experience at USP.
And even before I worked at USP, I actually served as a volunteer on a number of USP expert committees, evaluating proposed monographs for -- to go into the book.
And just from my experience, routine testing would not have picked up an impurity at that low of a level.
The fact that FDA had to resort to using mass spec -- using mass spec is a very sensitive detector to begin with, and they had to make that detector even more sensitive because they were looking at a single ion.
When you introduce a chemical into a mass spectrometer, it's ionized and then it breaks down into fragments. The initial ion is called the

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parent ion, and as it breaks down it forms daughter ions.
And that -- to be able to look at a single ion for NDEA or a single ion for NDMA increases the sensitivity of that method. So it's -- basically, I guess I would say it's -- compared to a routine GC or LC analysis, I would call it supercharged. It's many -- it's multiple times more sensitive than a routine procedure.
MR. DAVIS: I can't hear you, Jason.
VIDEO TECHNICIAN: The phone is on mute, I think.
The phone disconnected.
- - -
(Whereupon, a discussion off the record occurred.)
- - -
MR. DAVIS: Let's go off the record.
VIDEO TECHNICIAN: Going off the record. The time is 5:23 p.m.

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- - -
(Whereupon, a brief recess was taken.)
- - -
VIDEO TECHNICIAN: We are back on the record. The time is 5:29 p.m.
BY MR. REEFER:
Q. Dr. Sheinin, I understand that we were just disconnected from the phone line used for this Zoom deposition and that madam court reporter read back your prior answer.
Did you hear her recite that answer?
A. I did.
Q. Was there any additional information that you sought to provide in response to my previous question?
A. No.
Q. Has --
MR. DAVIS: Are you speaking, Jason, or did we lose you again?

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MR. REEFER: No, you haven't lost me yet, John. I was -- my wheels don't turn as fast as yours do, John, as you can probably tell.

BY MR. REEFER:

Q. Dr. Sheinin, has -- has FDA made statements indicating that the properties of nitrosamine impurities make them hard to detect in standard laboratory testing?

A. They have.

MR. DAVIS: Object to form. Object to the extent that it's not listed in his -- in the four corners of his report or reliance materials, whatever this is calling for, these statements.

BY MR. REEFER:

Q. With respect to your -- the opinion you offered regarding the capabilities of routine testing to detect levels of NDEA as found in some batches of Mylan's drug substance, is it relevant

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for you to compare the specification set forth in the compendium of not more than 0.1 percent versus the levels of NDEA detected in Mylan's drug?

A. Yes.

Q. How so?

A. The levels that are found in Mylan's API would be well below the .1 percent. So the testing of the impurity -- testing for impurities in the API, it would pass if -- unless -- unless there was another impurity of some unknown that was greater than .1 percent.

Q. And --

A. The NDEA or NDMA, if it was present, would be well below .1 percent.

Q. And just, I guess, for purposes of comparing apples to apples, does .1 percent translate to 1,000 parts per million?

A. Yes.

Q. And when I refer to routine testing, did you understand that to mean the high-performance liquid

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chromatography methods set forth and described in the monograph for valsartan?

A. Yes.

MR. REEFER: I don't have any further questions at this time, though I may, depending on whether or not Mr. Davis does.

MR. DAVIS: Okay. Just a few follow-ups, Dr. Sheinin. And I'll try to take them in the order in which they appeared.

- - -

EXAMINATION

- - -

BY MR. DAVIS:

Q. You testified to me earlier that you weren't an expert and not qualified to offer opinions on risk assessment; is that right?

A. Yeah. I'm not.

Q. So you wouldn't know how an in-process parameter could become what the FDA refers to as a critical quality attribute or a critical process

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parameter; is that right?

A. I -- I have an understanding of what critical quality parameters are. They are parameters that are critical to the manufacturing process. And --

Q. And the determination of their -- sorry, go ahead.

A. Go ahead.

Q. The determination of whether they are critical or not is through a risk assessment pursuant to ICH Q9, correct?

A. I believe it's in Q9.

Q. Okay. And do you have any idea of what the FDA expects in terms of inclusion in a DMF regarding critical quality attributes or critical process parameters?

A. I believe FDA expects them to be included in the description of the manufacturing process and the development report and so on.

Q. Okay. Thank you.

Counsel asked you some

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questions regarding routine testing.
Do you recall that? And whether GC-MS did something that would be considered routine testing or not?
MR. REEFER: Object to the form. Beyond the scope of my direct.
THE WITNESS: I recall he asked me questions about routine testing, and I would not consider GC-mass spec to be routine testing.
BY MR. DAVIS:
Q. When you say "routine testing," are you referring to routine testing that's done as part of, like, a USP monograph, like the specification and testing procedure for a USP monograph or an approved DMF specification or ANDA spec?
A. Or NDA spec. All of that.
Q. Right. But an already-approved specification, correct?
A. No. A company that's

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submitting an ANDA or an NDA today, for the most part, will be using routine analytical procedures.
GC-mass spec is not anything that I would consider routine.
Q. Even though the FDA expects it to be done when unknown impurities are found?
A. I'm not aware that the FDA said you have to use GC-mass spec anytime there's an unknown impurity.
I'm aware that the method that FDA published for valsartan impurities -- nitrosamine impurities in valsartan is a GC-mass spec method. But I'm not aware that FDA has said that any unknown has to be looked at by GC-mass spec.
Q. You are aware that the DEA requires manufacturers to evaluate unknown impurities?
Are you aware of that?
MR. REEFER: Object to form. Misstates the testimony.

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But go on.
THE WITNESS: According to ICH Q3A and Q3B, companies are -- well, as I said earlier, FDA considers ICH guidance as recommendations. So, accordingly, FDA is recommending that those two guidances be followed in terms of determine -- making a determination of the impurities in a given API or a drug product.
I don't see anywhere in those guidances where ICH says you have to use GC-mass spec.
BY MR. DAVIS:
Q. I'm talking about the FDA requiring manufacturers to evaluate unknown impurities.
Are you aware of that obligation?
A. I'm not -- I'm not aware of a specific guidance that says -- anything beyond what's in Q3A or Q3B as to how to -- not how to, but as to what the

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criteria would be for reporting and identifying those impurities.
MR. DAVIS: I'm marking Tab 16 as Exhibit-19.
- - -
(Whereupon, Exhibit Sheinin-19, No Bates, Warning Letter, Mylan Laboratories Limited – Unit 7, was marked for identification.)
- - -
MR. REEFER: I'll take a -- will you give me a standing objection, John, to the use of this exhibit on the basis that it's beyond the scope of my direct and, also, it does not apply to any facility that's been deemed to be at issue in this litigation?
MR. DAVIS: Standing objection granted, but also disagreed with.
MR. REEFER: Very lawyerly.
BY MR. DAVIS:

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Q. You told me earlier, Dr. Sheinin, you hadn't looked at anything related to Unit 7; is that right?
A. That's right.
Q. Okay. Do you recognize this as a warning letter that was issued to Unit 7 in August of 2020?
MR. REEFER: Objection. Beyond the scope.
THE WITNESS: Yes.
BY MR. DAVIS:

[redacted]

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[redacted]

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[redacted]

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[redacted]

BY MR. DAVIS:
Q. You wouldn't think it relevant to know what the FDA has been advising manufacturers their obligations are regarding analytical testing --
MR. REEFER: Object to form.
BY MR. DAVIS:
Q. -- specifically as it relates to nitrosamines?

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MR. REEFER: Object to form. Misstates the document. Beyond the scope. Foundation.

Go ahead.

THE WITNESS: I have no idea whatsoever what FDA has asked any other defendant in this case. I have no way of knowing that.

It's -- I mean, you know it. But I have no way to know that. How would you think I would know that?

BY MR. DAVIS:

[redacted]

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[redacted]

So I don't require a response to that question, but -- or statement, rather.

MR. REEFER: Object to the colloquy.

BY MR. DAVIS:

Q. But let me ask you this, Dr. Sheinin.

Is one of the ways to thoroughly evaluate an unknown peak in a GC FID by doing GC-MS?

MR. REEFER: Object to form. Beyond the scope. Beyond the direct.

Go ahead, Dr. Sheinin, if you know.

THE WITNESS: It's one

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possible way.

BY MR. DAVIS:

Q. Okay. Would it be the most prevalent possible way in terms of evaluating unknown peaks that appear in a GC FID?

MR. REEFER: Same objection.

THE WITNESS: It would be a very good way. I guess partly it depends on if -- if the material -- well, it's one way -- GC-mass spec would be one way to evaluate a peak coming out of a GC that's an unknown by flame-ionization detection.

But we've been talking here about solvents and recovered solvents. When you mentioned the API, my question is, are you talking about, when you talk about an API, the assay? Are you talking about the impurity test that's in the specification or in the USP monograph? Or are you

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talking about a solvent?

There's -- there's a world of differences in how you go about testing for unknowns in the API versus these nitrosamines. So there's -- I just feel that you were not specific enough in what you were asking me.

BY MR. DAVIS:

Q. Okay. Well, I think you've answered my question, which is, GC-MS is a prevalent way to thoroughly evaluate an unknown peak in a GC, correct?

A. My premise was that I do not consider GC-mass spec to be a routine procedure. And I stand by that. I do not consider it to be routine.

Q. You don't consider it to be routine in -- as a procedure that's in an approved specification, that's right.

Is that what your testimony is?

A. Yes.

Q. Okay.

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A. It may -- it may be in an approved specification today because of nitrosamines. But I do not consider it to be routine.
Q. In an approved specification?
A. In an approved specification or in an application for marketing approval.
Q. You don't think that it's routine that all the workup in a DMF that goes into an ANDA application or drug master file for a product that's to be approved, you don't think that it's routine that companies -- manufacturers do GC-MS?
MR. REEFER: Objection. Asked and answered.
THE WITNESS: I do not consider it to be a routine quality control test.
BY MR. DAVIS:
Q. Okay. A routine quality control test. Okay.

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A. Well, you're talking about quality control of a product. It's not a -- it's not a routine test.
Q. Right. But quality control is analytical chemistry for an approved product, right?
A. Or it's a proposed specification for inclusion in an application of an ANDA or NDA. It's the same thing. It's still -- it's a quality control test.
Q. Are you aware that --
A. That we're talking about.
Q. Are you aware that Mylan's own toxicologist testified to me that he gets about, like, 3 to 4,000 requests for GC-MS per year?
Did you review Lance Monar's testimony? It wasn't even provided to you, was it?
MR. REEFER: Object to form. Foundation. Beyond the scope.
THE WITNESS: I'd have to look on the list in Appendix B.

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But as I said earlier, I have not reviewed any of those testimonies from anybody from Mylan.
BY MR. DAVIS:
Q. Okay. And that would include, also, Derek Glover's testimony; you haven't reviewed any of his, even though it is listed on Exhibit B, right?
MR. REEFER: Objection. Literally just answered.
But go ahead, Dr. Sheinin.
THE WITNESS: I have not reviewed any testimony from anybody at Mylan.
BY MR. DAVIS:


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BY MR. DAVIS:
Q. Okay. Thank you.
You told Mr. Reefer that even a -- a Mylan valsartan product that had 1.57 parts per million NDEA would still meet compendial standards because unknown impurities are controlled in the USP monograph at not more than .1 percent, which is 1,000 parts per

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million, right?
A. I believe I qualified that also by saying in the specification in the approved application as well.
Q. So why did the recalls even happen, then, if that's what -- if NDEA was only to be controlled at not less than 1,000 parts per million, which appears to be your expert opinion, why are we here? Why did these recalls happen?
A. I did not -- I did not say that -- I forget what your question was already. It's been a long day.
Can you repeat your question?
Q. Sure. And I appreciate it's been a long day.
You testified to Mr. Reefer, in response to one of his questions, that a Mylan valsartan product containing 1.57 parts per million NDEA would still meet compendial -- the USP monograph for valsartan which controlled any other

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impurities at .1 percent; is that right?
A. Yes.
Q. So if that's the case, why did the recalls happen? Can you tell me that?
MR. REEFER: Object to form. Beyond the scope. Beyond the redirect.
THE WITNESS: The recalls happened because FDA was told that there were nitrosamines in some products, and FDA's investigation showed that there was -- there was a theoretical risk and, ultimately, they determined that there needs to be a lower acceptance criteria for nitrosamines. And they called it the acceptable intake level.
And there had to be a development of more sensitive analytical procedures to be able to detect and quantify those nitrosamines.

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So that's why there was a recall, and I -- I would expect that companies manufacturing these products will have to include testing for nitrosamines in their specification as a -- doing a supplement to their approved application.
So there would be an additional test beyond what's in the USP. And I would hope that companies would submit the same information to USP, for USP to be able to update the monograph for all of the sartans.
BY MR. DAVIS:
Q. So why does it even matter that USP monograph had a not more than .1 percent limit, if that's not even the limit that applied to nitrosamines at any point?
MR. REEFER: Object to form. Object to form. It misstates the testimony.

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THE WITNESS: I don't -- I just don't understand your question. It's --
BY MR. DAVIS:
Q. Well, I don't understand your report.
MR. REEFER: Come on.
MR. DAVIS: Let me ask it again. Let me ask it again.
BY MR. DAVIS:
Q. Why would it be important for you, in your report, that the USP monograph had a not more than .1 percent limit for other impurities if that's not even the limit that applied to nitrosamines at any point? Why is that relevant to your report?
MR. REEFER: Objection to form. Misstates the testimony.
But go ahead, Doctor.
THE WITNESS: I'm totally confused by now.
The USP monograph is recognized in the Food, Drug and

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Cosmetic Act as being an official compendium. And that monograph has to be met in order for a product not to be considered adulterated.

That's why the monograph is important. And that's why the acceptance criteria in the specification for unknown impurities is important.

BY MR. DAVIS:

Q. Have you looked at what the -- what the definition of adulterated is in the FD&C Act at all recently?

A. Yes, I have. I believe I have it in my report.

Q. Okay. And so you'll agree with me, then, that a product is adulterated if it's manufactured in a way where the manufacturer could not assure that it would -- well, let me just read you the language so I'm not confused or misstating it.

MR. REEFER: What are you

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reading from, John?

MR. DAVIS: 21 USC 351.

BY MR. DAVIS:

Q. A drug or device shall be deemed adulterated --

A. Wait. Wait.

MR. REEFER: Hold on. He said 21 USC 351.

THE WITNESS: Okay. I thought you said USP.

MR. DAVIS: 21 USC 351, United States Code.

BY MR. DAVIS:

Q. A drug or a device shall be adulterated, if it is a drug, and the methods used in, or the facilities or controls used for, its manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the

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quality and purity characteristics which it purports or is represented to possess.

Have you seen that language before?

A. Yes.

Q. Okay. So you agree with me, then, that a drug is adulterated if it's manufactured out of compliance with GMP, correct?

MR. REEFER: Object to form. Object to form. Beyond the scope.

THE WITNESS: The -- that definition is -- I want to look at the definition I copied into my report.

MR. REEFER: He's quoting from a different subsection.

THE WITNESS: Oh, okay. Can you read that again?

MR. DAVIS: Sure.

BY MR. DAVIS:

Q. A drug or a device shall be deemed to be adulterated -- and then this is A1 -- or A2B, Subsection A2B, If it is

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a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements in this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics which it purports or is represented to possess.

Do you agree with me that that's -- that's a definition of an adulterated drug, a situation in which a drug becomes adulterated, per federal law?

A. Yes.

Q. Okay. And, in fact, that's what Mylan was told in its November 2019 Unit 8 warning letter, Exhibit-3, was it not?

MR. REEFER: Objection.

BY MR. DAVIS:

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Q. We saw that language, right?
MR. REEFER: Object to form. You've covered this in cross. You know, asked and answered.
But go ahead.
THE WITNESS: And yet FDA, within a short period of time, allowed Mylan to reintroduce their valsartan. So there was no legal action taken, as far as I know, about the valsartan that was the subject of that inspection.
BY MR. DAVIS:
Q. Okay. And for about the umpteenth time today, you have no idea how that valsartan that was brought back to the market differed from the valsartan that Mylan had to recall?
MR. REEFER: As acknowledged by the question itself, asked and answered.
BY MR. DAVIS:
Q. Is that a yes?
A. Yes.

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Q. Okay. Last questions.
Mr. Reefer asked you some questions about procurements of API, I believe, from multiple sources and how that might affect the quality or purity characteristics of the product.
Do you remember that discussion with him?
A. Yes.
Q. Okay. Do you have an understanding that under FDA regulations that a manufacturer like Mylan is responsible for all of its suppliers?
MR. REEFER: Object to form. Beyond the scope.
THE WITNESS: That Mylan is responsible for all of their suppliers? And to what extent and to what regard?
I think that's a -- like an unfinished question.
BY MR. DAVIS:
Q. Sure.
If Mylan, for example,

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procures raw materials from a vendor, a raw material vendor, and that vendor is out of GMP compliance and the raw materials it's sending to Mylan are no good, it's ultimately Mylan's responsibility to adequately vet its vendors.
Isn't that the FDA's position as stated in regulations, and GMP regulations specifically?
MR. REEFER: Object to form.
BY MR. DAVIS:
Q. Do you have any understanding of that?
MR. REEFER: Object to form. Beyond the scope of his report. Beyond the scope of my direct.
But, I don't know, go ahead.
THE WITNESS: Yes. Mylan would be responsible for their suppliers.
MR. DAVIS: Okay. That's all the questions I have.
MR. REEFER: So we'll go

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huddle, and I'll come back to see if -- I'm just kidding, John.
VIDEO TECHNICIAN: No more questions?
MR. DAVIS: We can go off the record.
MR. REEFER: No. I have --
MR. DAVIS: Sorry, I take it back.
MR. REEFER: I just had -- I just have maybe two questions, three questions.
- - -
EXAMINATION
- - -
BY MR. REEFER:
Q. Dr. Sheinin, do you purport to offer any opinions with respect to whether Mylan complied with GMP regulations?
A. No.
Q. Do you intend to offer any opinion with respect to whether Mylan's investigation of unknown peaks, in some

form or fashion, complied with rules and regulations?

A. No.

Q. To your knowledge, did what's been described as Mylan Unit 7 manufacture API -- API valsartan?

A. I have no idea what Unit 7 manufactures.

MR. REEFER: All right. I think that's all I have.

MR. DAVIS: No further questions.

VIDEO TECHNICIAN: This marks the end of today's deposition. The time is 6:06 p.m.

- - -

(Whereupon, the deposition concluded at 6:06 p.m.)

- - -

CERTIFICATE

I, Amanda Maslynsky-Miller, Certified Realtime Reporter, do hereby certify that prior to the commencement of the examination, ERIC SHEININ, Ph.D., was remotely sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by me at the time, place and on the date hereinbefore set forth, to the best of my ability.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

_____
Amanda Miller
Certified Realtime Reporter
Dated: March 31, 2022

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ERRATA

PAGE	LINE	CHANGE/REASON

ACKNOWLEDGMENT OF DEPONENT

I,____________________, do hereby certify that I have read the foregoing pages, 1 - 318, and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

____

ERIC SHEININ, Ph.D. DATE

Subscribed and sworn
to before me this
_____ day of ______________, 20____.

My commission expires:______________

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Notary Public

LAWYER'S NOTES

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